US009329111B2

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Ebi et al.

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(54) **SAMPLE PREPARATION APPARATUS**

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(73) Assignee: **SYSMEX CORPORATION**, Kobe-shi (JP)

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(21) Appl. No.: **13/007,331**

(22) Filed: **Jan. 14, 2011**

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(30) **Foreign Application Priority Data**

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Mar. 23, 2010 (JP) 2010-066405

(51) **Int. Cl.**

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B01D 45/00	(2006.01)
B01D 35/00	(2006.01)
G01N 1/40	(2006.01)
G01N 15/14	(2006.01)
G01N 35/00	(2006.01)

(52) **U.S. Cl.**

CPC ***G01N 1/4077*** (2013.01); *G01N 15/14* (2013.01); *G01N 2001/4088* (2013.01); *G01N 2035/00495* (2013.01)

(58) **Field of Classification Search**

CPC G01N 1/34; G01N 2001/4088; G01N 15/147; G01N 15/1475; G01N 1/4077; G01N 2015/1006; G01N 2015/1493; G01N 35/1095; G01N 15/1459; G01N 15/14; G01N 15/1429; G01N 15/1434; G01N 1/38; G01N 1/40; G01N 2035/00495; G01N 33/4833; G01N 33/57496; G01N 35/00613; G01N 35/02; B01L 2200/0647; B01L 2200/14; B01L 2200/143; B01L 2300/0681; B01L 2300/0832; B01L 2300/0858; B01L 3/502; B01L 3/52

USPC 422/72, 50, 415, 68.1, 500–504, 506, 422/513, 527, 533, 534, 209, 258, 259, 269, 422/271; 702/127, 142, 145

See application file for complete search history.

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Primary Examiner — Dean Kwak
(74) *Attorney, Agent, or Firm* — Mots Law, PLLC

(57) **ABSTRACT**

A sample preparation apparatus comprising: a filter which separates predetermined cells from a liquid sample containing a plurality types of cells; a rotor which includes a magnetic body and detaches the predetermined cells attached to the filter by rotation; a driving unit which rotates the rotor using a magnetic force; and a rotation information acquiring unit which acquires a rotation information of the rotor when the driving unit rotates the rotor. A method and a computer program product are also disclosed.

19 Claims, 20 Drawing Sheets

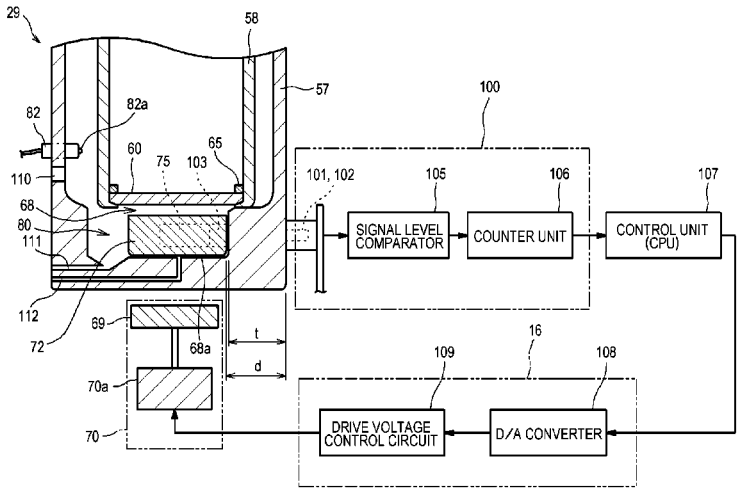


FIG. 1

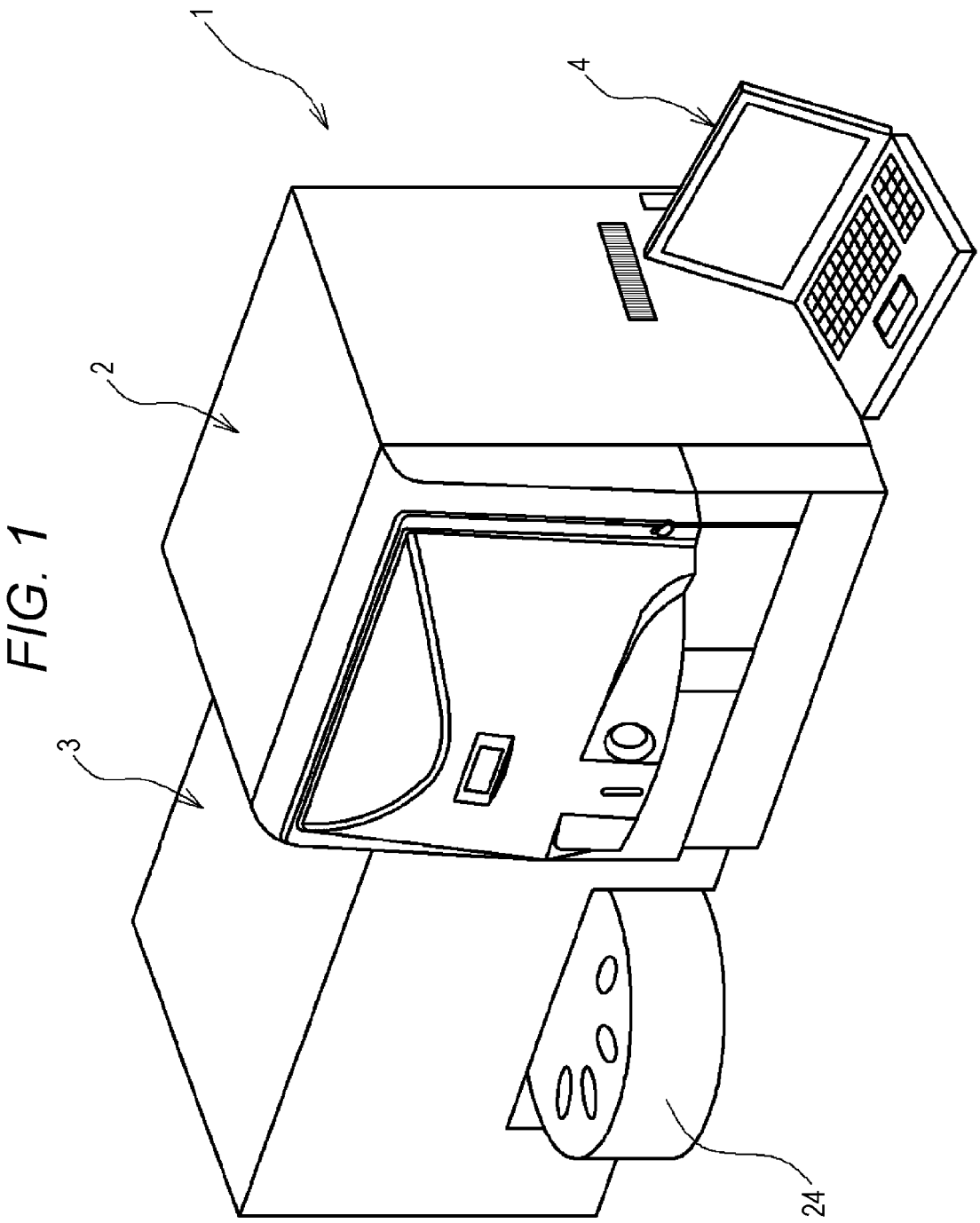


FIG. 2

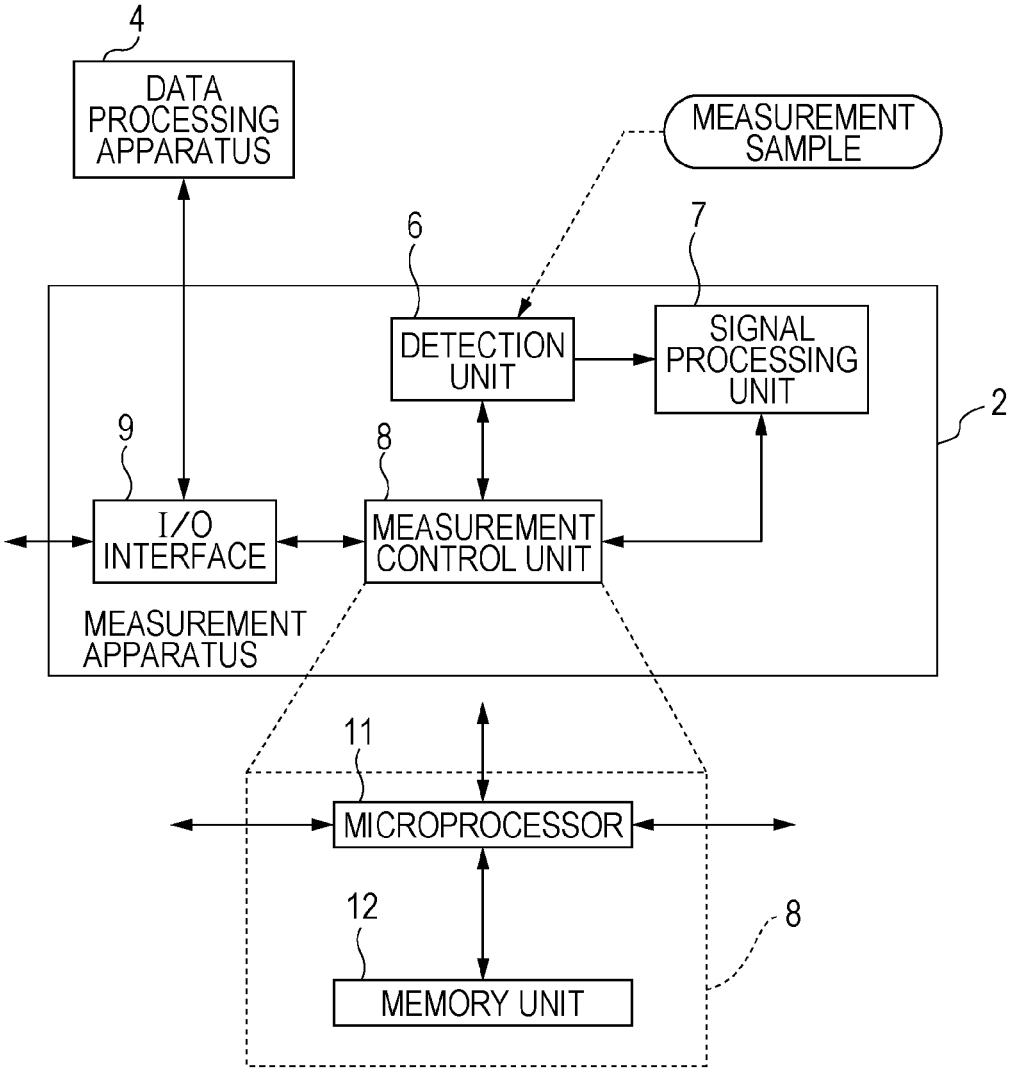

4
DATA PROCESSING APPARATUS
MEASUREMENT SAMPLE
6
7
DETECTION UNIT
SIGNAL PROCESSING UNIT
2
9
8
I/O INTERFACE
MEASUREMENT CONTROL UNIT
MEASUREMENT APPARATUS
11
MICROPROCESSOR
12
8
MEMORY UNIT

FIG. 3

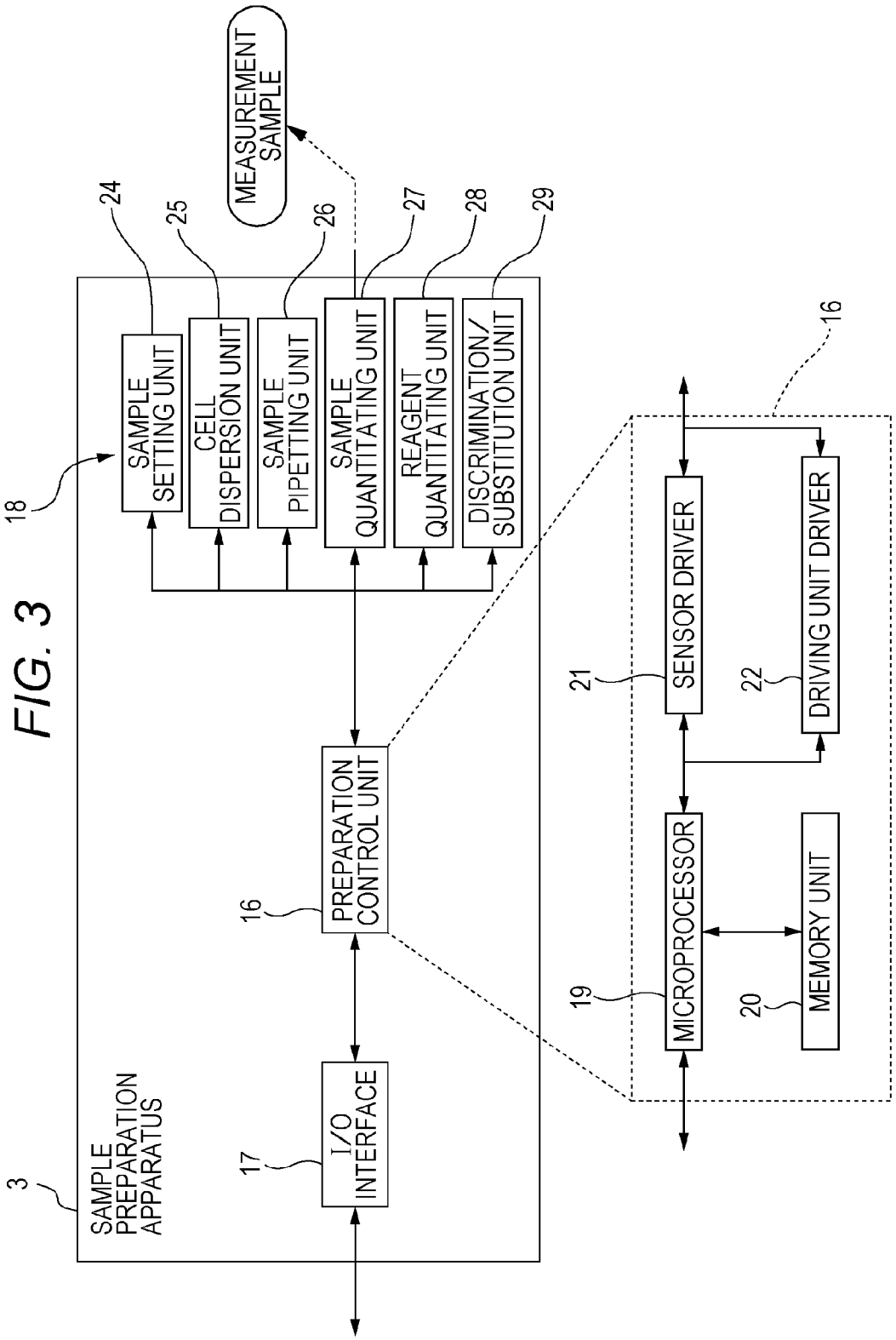

MEASUREMENT SAMPLE
24
25
26
27
28
29
18
SAMPLE SETTING UNIT
CELL DISPERSION UNIT
SAMPLE PIPETTING UNIT
SAMPLE QUANTITATING UNIT
REAGENT QUANTITATING UNIT
DISCRIMINATION/ SUBSTITUTION UNIT
16
PREPARATION CONTROL UNIT
17
I/O INTERFACE
3
SAMPLE PREPARATION APPARATUS
16
21
SENSOR DRIVER
22
DRIVING UNIT DRIVER
19
MICROPROCESSOR
20
MEMORY UNIT

FIG. 4

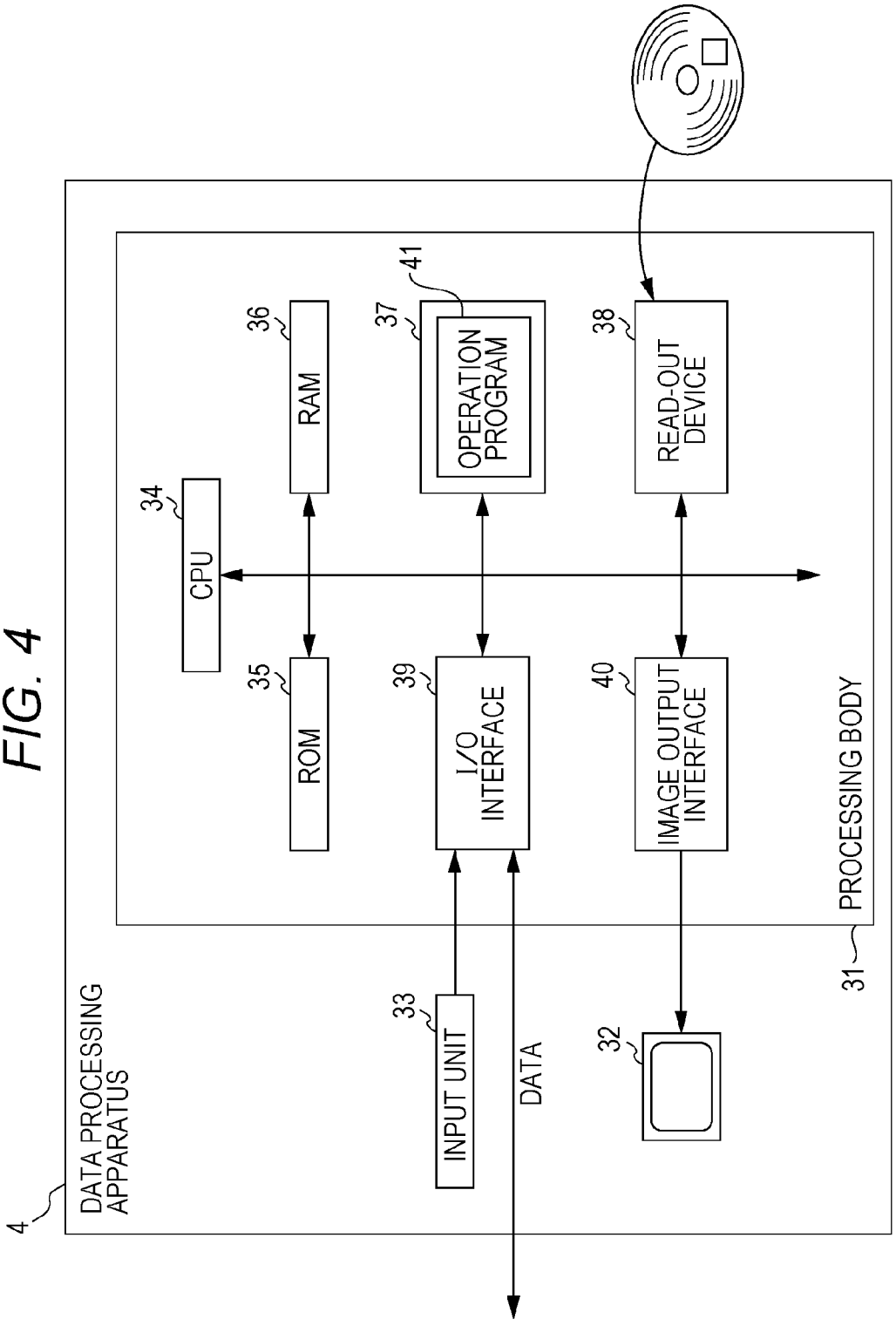

4
DATA PROCESSING APPARATUS
31
PROCESSING BODY
CPU
34
ROM
35
RAM
36
I/O INTERFACE
39
OPERATION PROGRAM
37
41
IMAGE OUTPUT INTERFACE
40
READ-OUT DEVICE
38
INPUT UNIT
33
32
DATA

FIG. 5

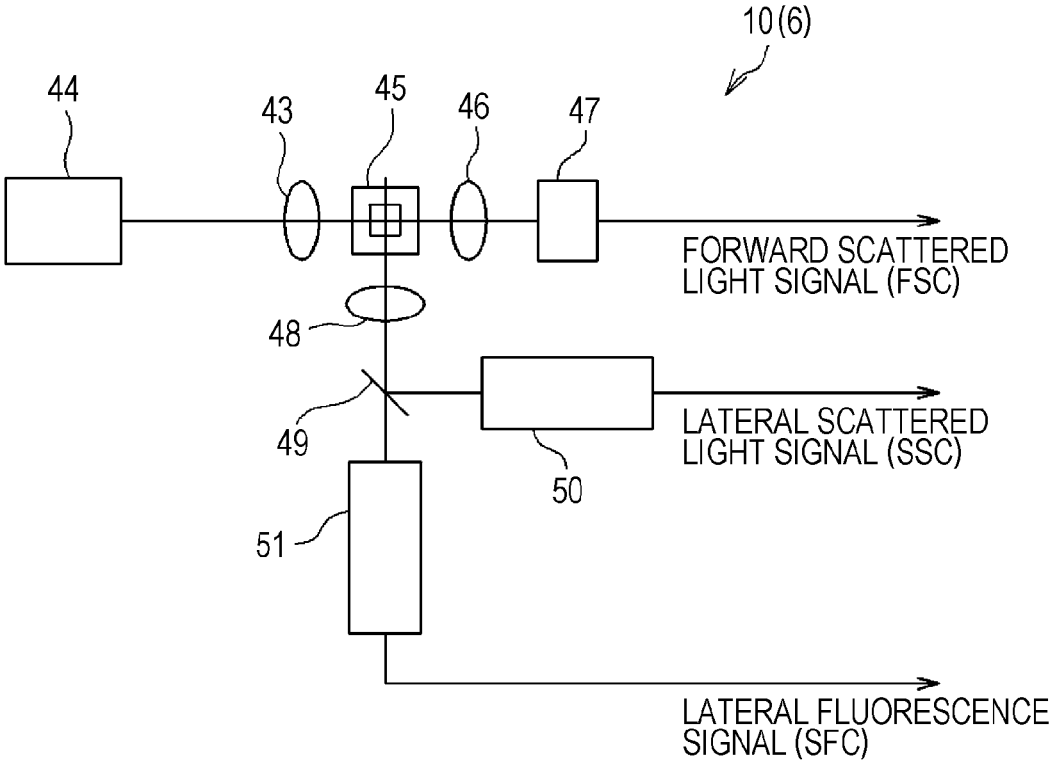

10(6)
44
43
45
46
47
FORWARD SCATTERED LIGHT SIGNAL (FSC)
48
49
LATERAL SCATTERED LIGHT SIGNAL (SSC)
50
51
LATERAL FLUORESCENCE SIGNAL (SFC)

FIG. 6

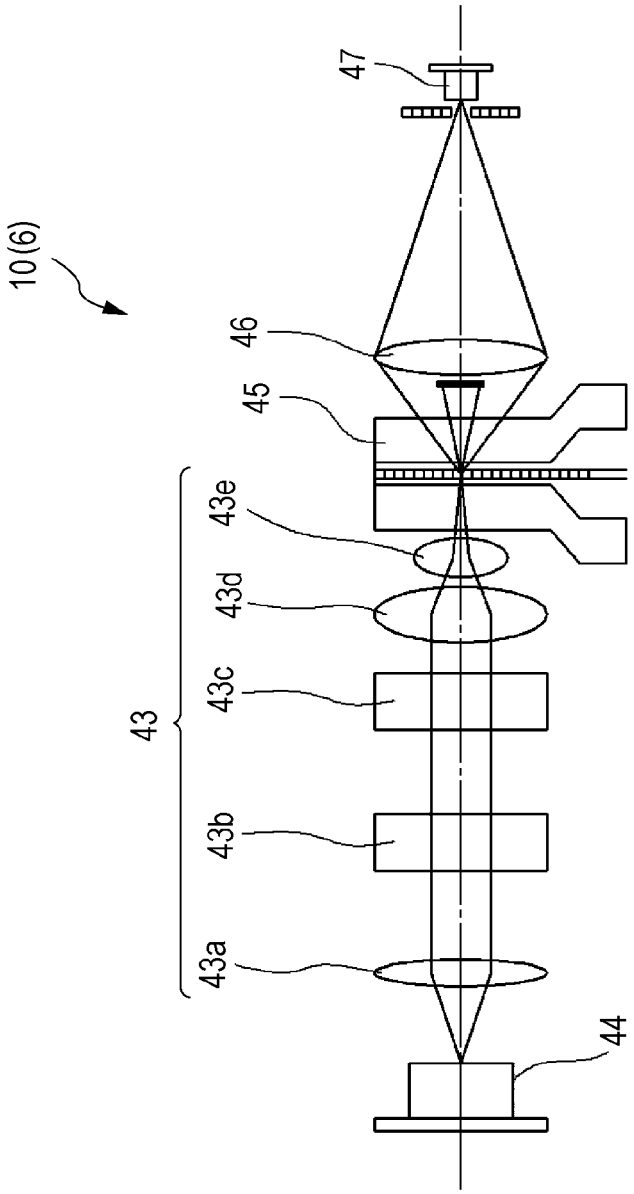


FIG. 7

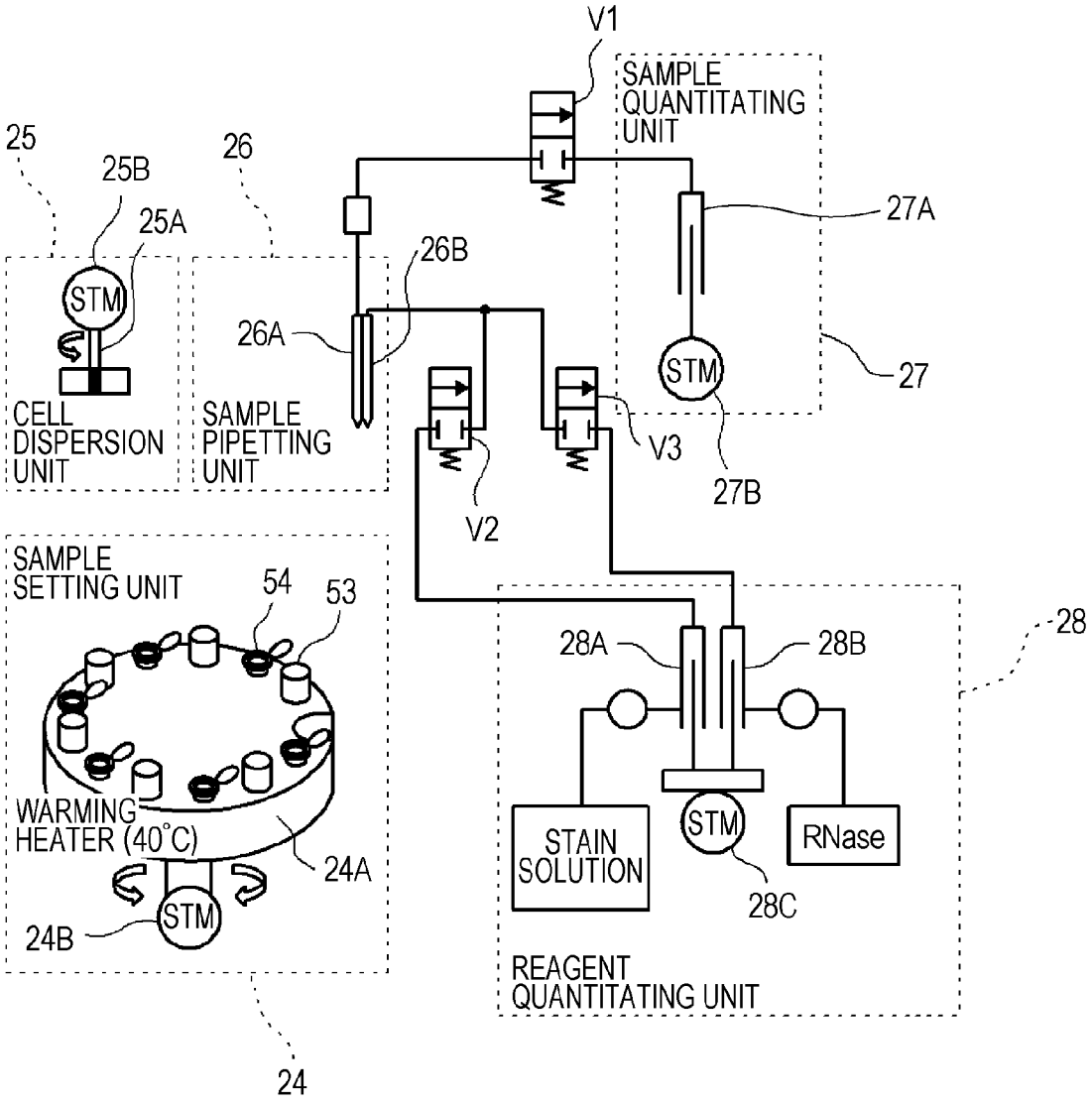

V1
SAMPLE QUANTITATING UNIT
25
25B
25A
26
26B
26A
27A
27
STM
CELL DISPERSION UNIT
SAMPLE PIPETTING UNIT
V2
V3
27B
SAMPLE SETTING UNIT
54
53
WARMING HEATER (40°C)
24A
24B
24
28
28A
28B
STAIN SOLUTION
RNase
28C
REAGENT QUANTITATING UNIT

FIG. 8

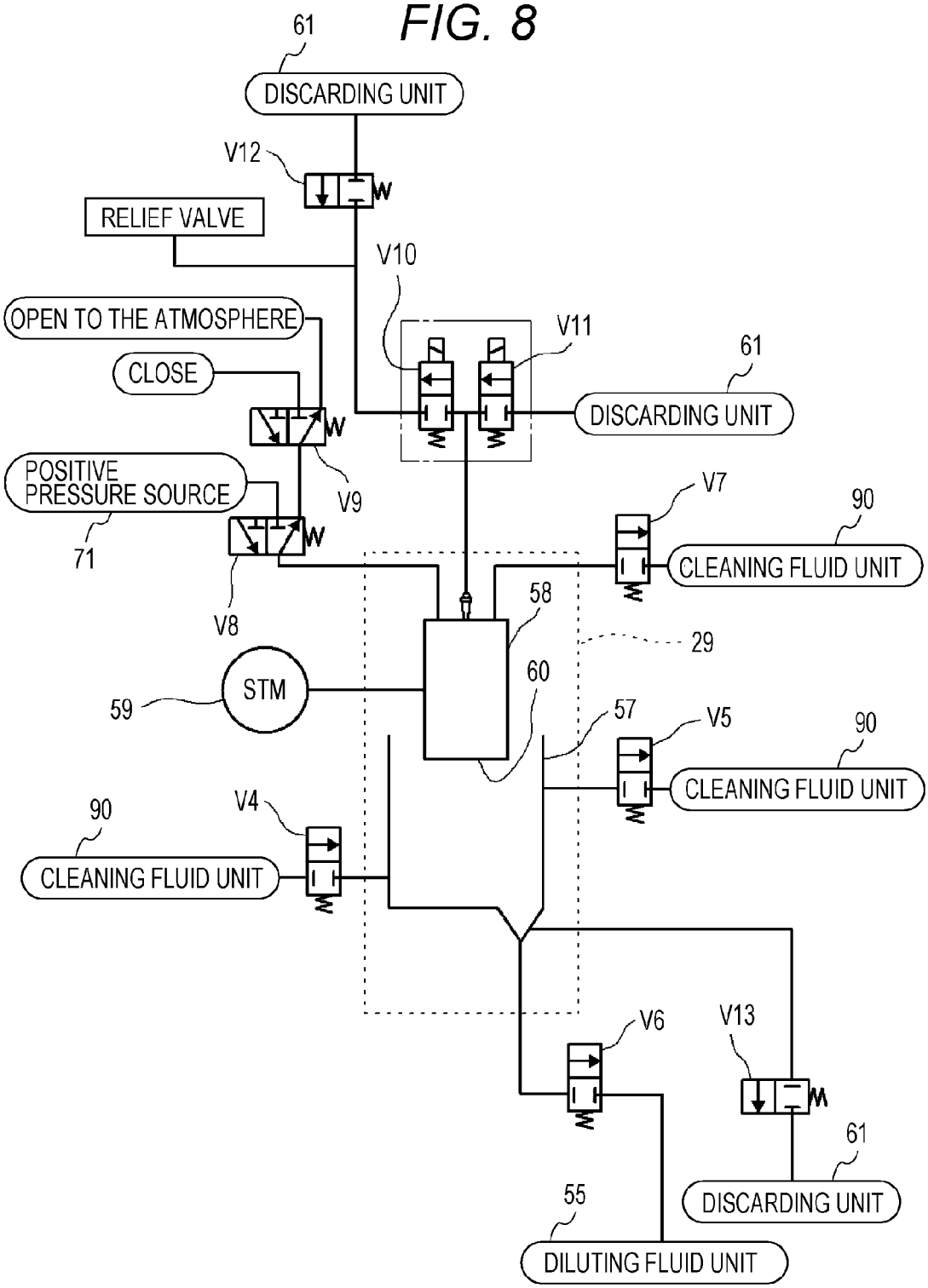

61
DISCARDING UNIT
V12
RELIEF VALVE
V10
OPEN TO THE ATMOSPHERE
V11
61
CLOSE
DISCARDING UNIT
POSITIVE PRESSURE SOURCE
V9
V7
90
71
CLEANING FLUID UNIT
V8
58
29
STM
59
60
57
V5
90
CLEANING FLUID UNIT
90
V4
CLEANING FLUID UNIT
V6
V13
61
55
DISCARDING UNIT
DILUTING FLUID UNIT

FIG. 9

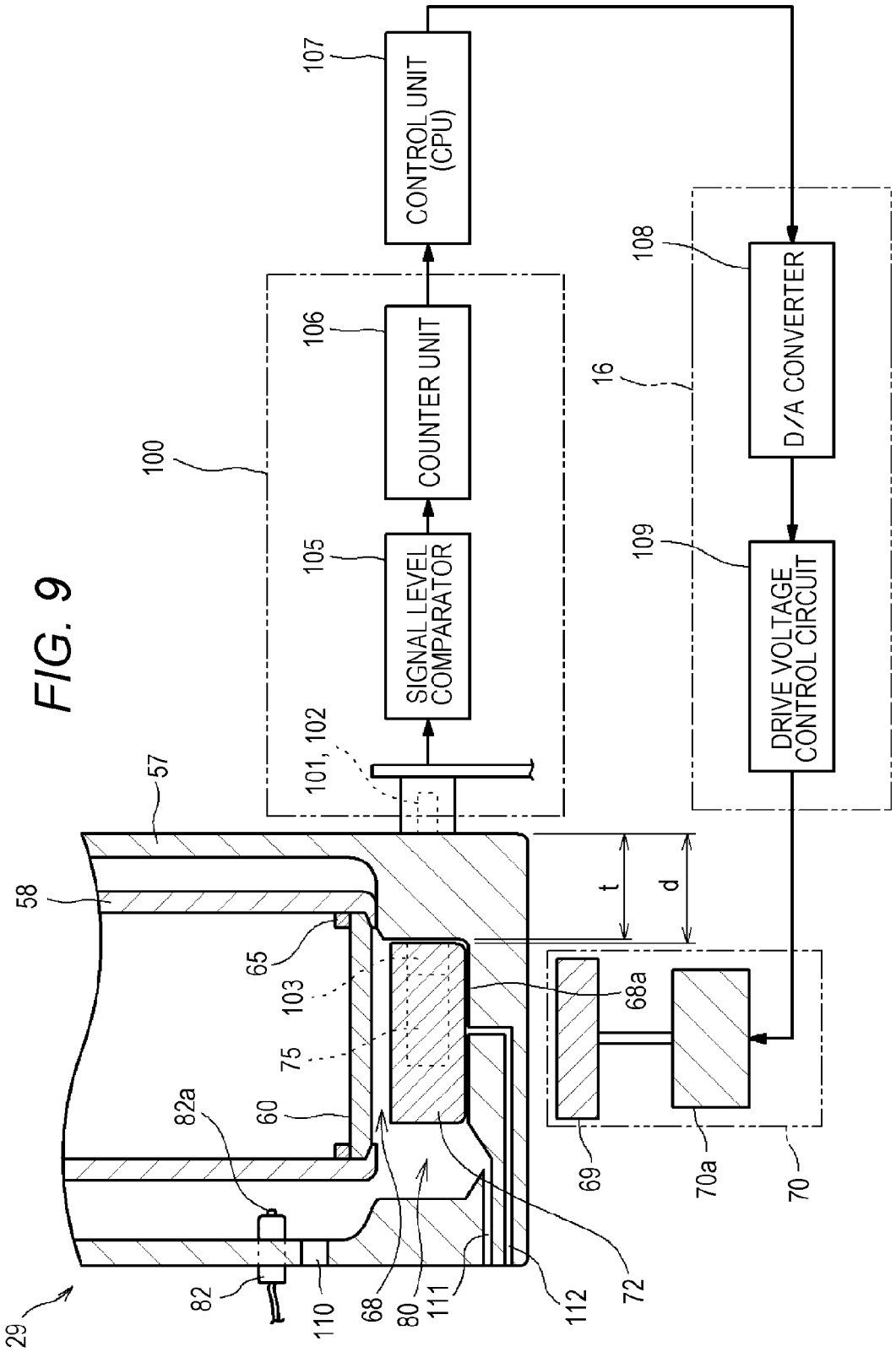

CONTROL UNIT (CPU)
107
COUNTER UNIT
106
SIGNAL LEVEL COMPARATOR
105
101, 102
100
D/A CONVERTER
108
DRIVE VOLTAGE CONTROL CIRCUIT
109
16
57
58
65
103
75
60
82a
82
110
68
80
111
112
72
68a
69
70a
70
29
t
d

FIG. 10

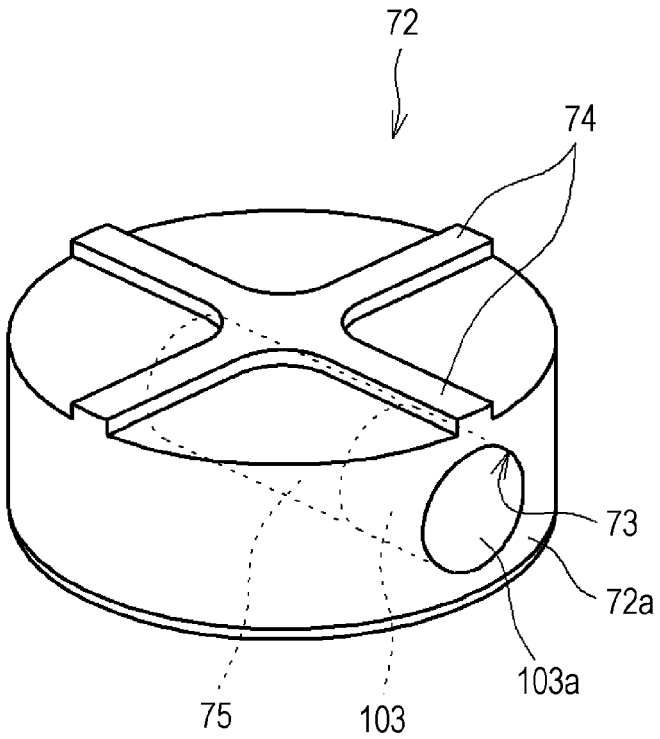


FIG. 11A

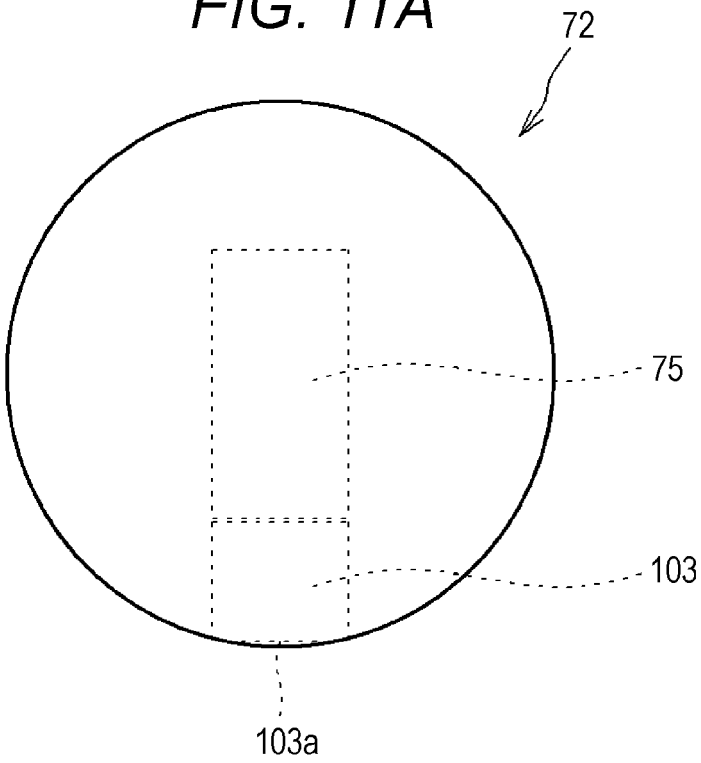


FIG. 11B

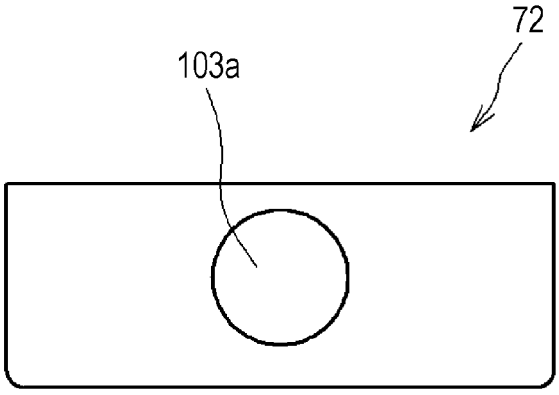


FIG. 12

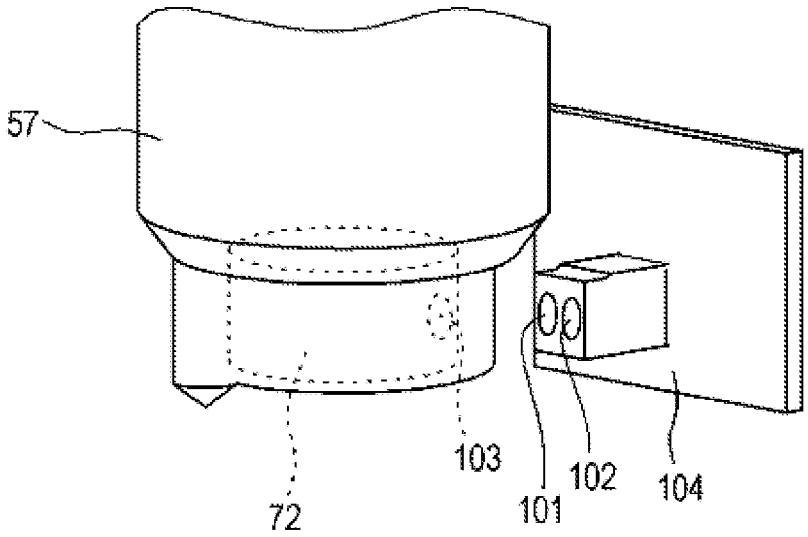


FIG. 13

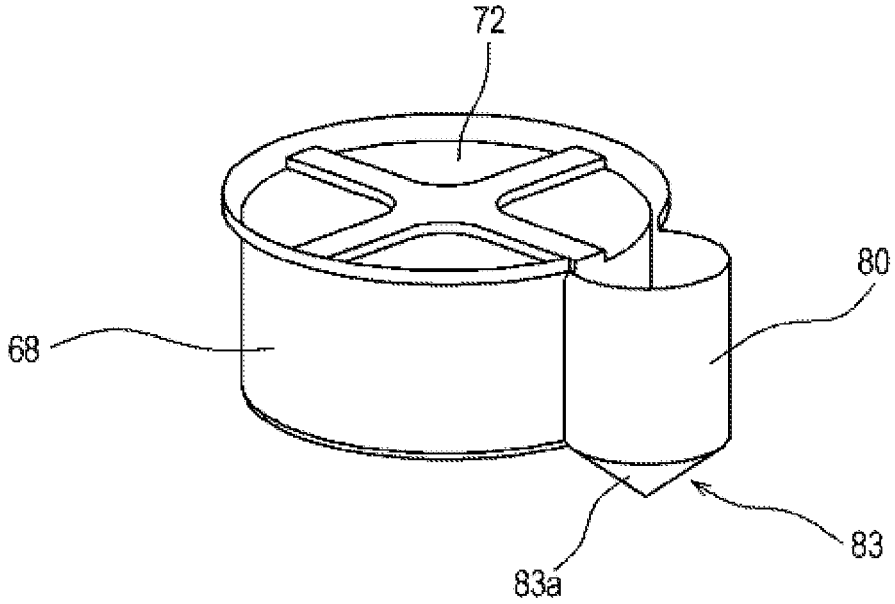


FIG. 14A

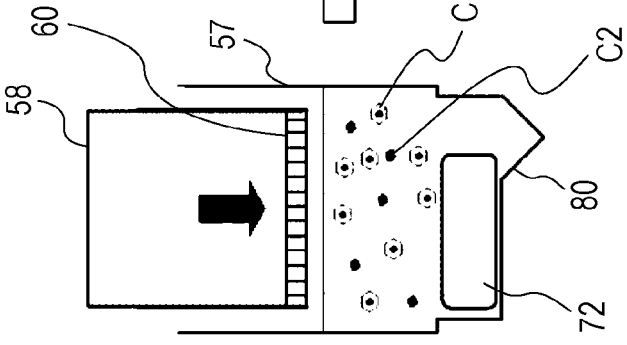


FIG. 14B

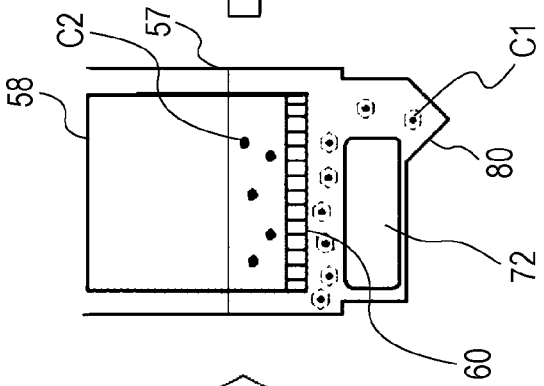


FIG. 14C

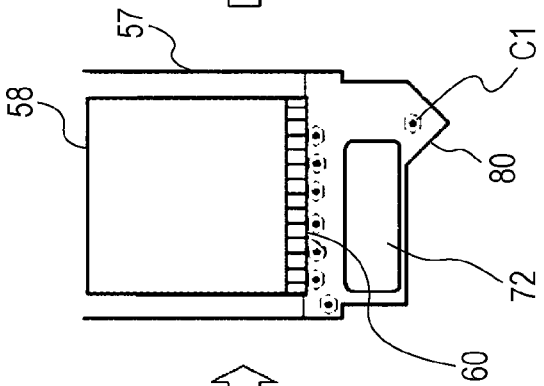


FIG. 14D

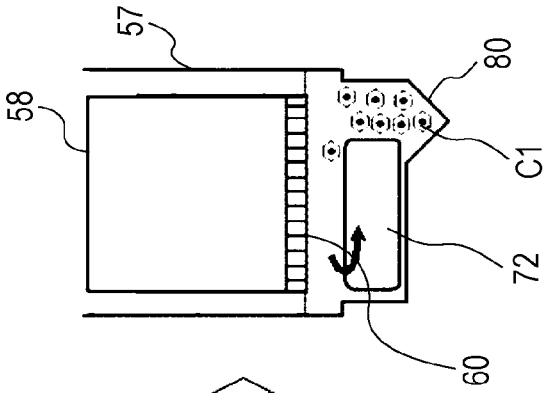


FIG. 15

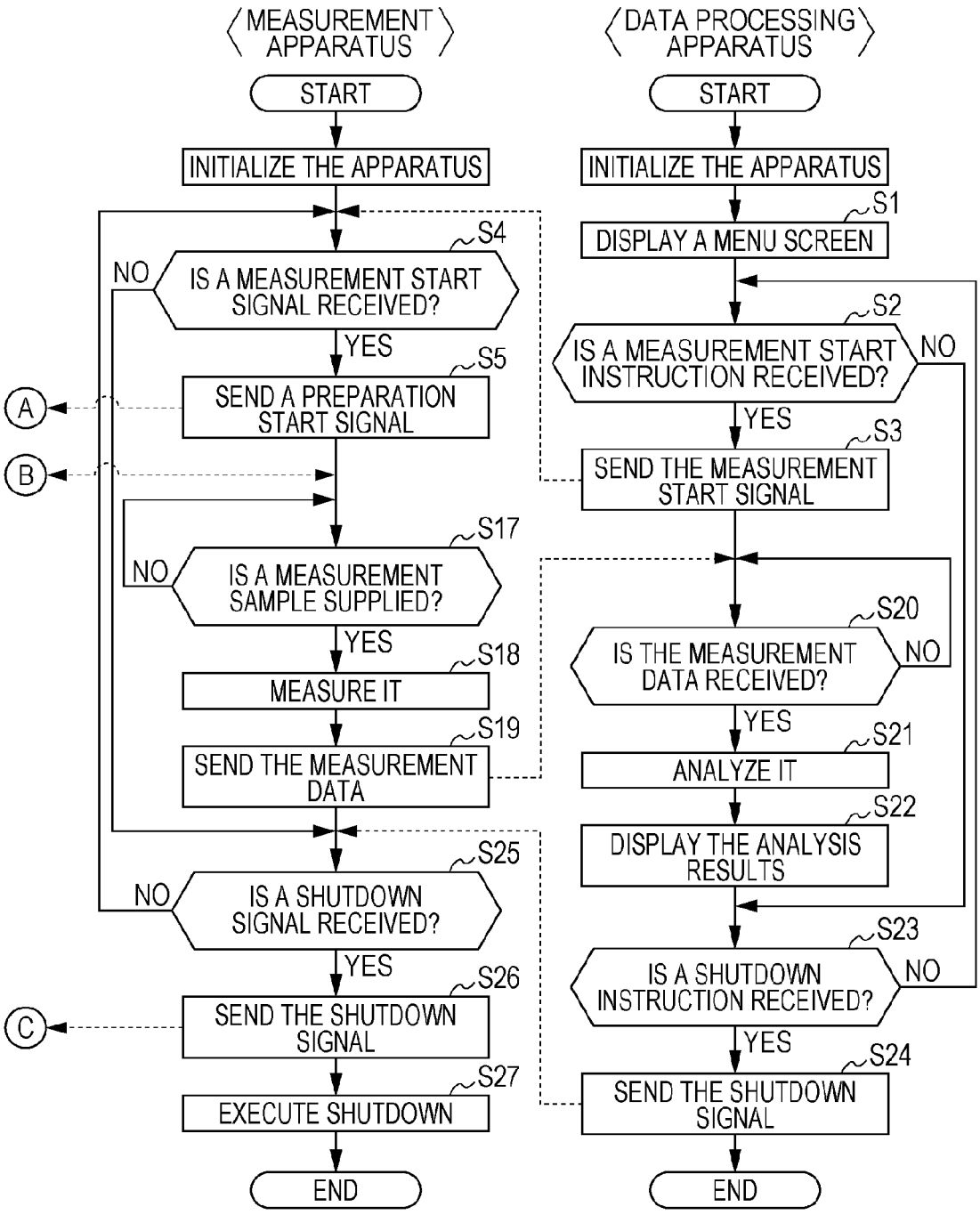

MEASUREMENT APPARATUS
START
INITIALIZE THE APPARATUS
S4
IS A MEASUREMENT START SIGNAL RECEIVED?
NO
YES
S5
SEND A PREPARATION START SIGNAL
A
B
S17
IS A MEASUREMENT SAMPLE SUPPLIED?
NO
YES
S18
MEASURE IT
S19
SEND THE MEASUREMENT DATA
S25
IS A SHUTDOWN SIGNAL RECEIVED?
NO
YES
S26
SEND THE SHUTDOWN SIGNAL
C
S27
EXECUTE SHUTDOWN
END
DATA PROCESSING APPARATUS
START
INITIALIZE THE APPARATUS
S1
DISPLAY A MENU SCREEN
S2
IS A MEASUREMENT START INSTRUCTION RECEIVED?
NO
YES
S3
SEND THE MEASUREMENT START SIGNAL
S20
IS THE MEASUREMENT DATA RECEIVED?
NO
YES
S21
ANALYZE IT
S22
DISPLAY THE ANALYSIS RESULTS
S23
IS A SHUTDOWN INSTRUCTION RECEIVED?
NO
YES
S24
SEND THE SHUTDOWN SIGNAL
END

FIG. 16

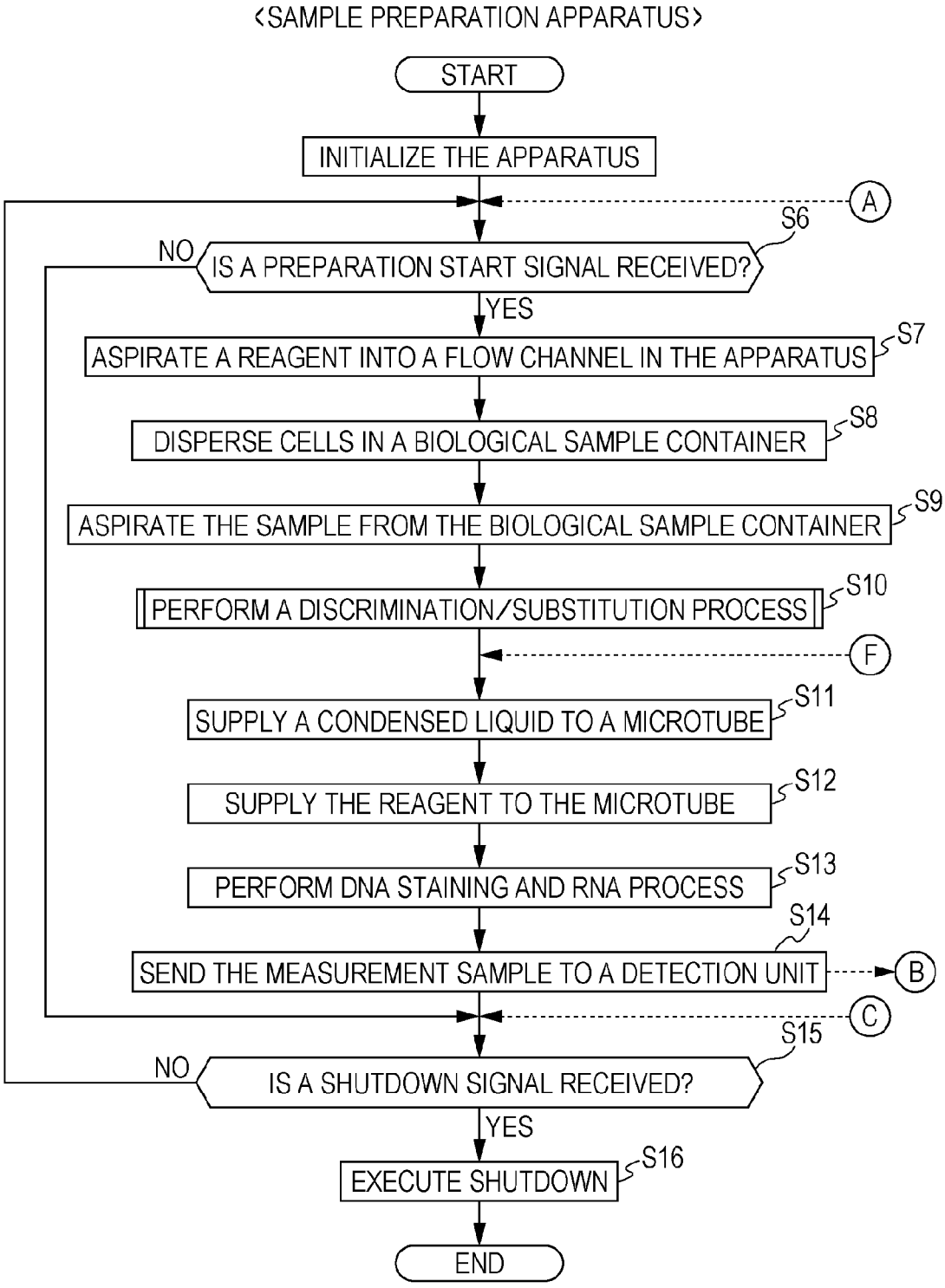

<SAMPLE PREPARATION APPARATUS>
START
INITIALIZE THE APPARATUS
A
S6
NO
IS A PREPARATION START SIGNAL RECEIVED?
YES
S7
ASPIRATE A REAGENT INTO A FLOW CHANNEL IN THE APPARATUS
S8
DISPERSE CELLS IN A BIOLOGICAL SAMPLE CONTAINER
S9
ASPIRATE THE SAMPLE FROM THE BIOLOGICAL SAMPLE CONTAINER
S10
PERFORM A DISCRIMINATION/SUBSTITUTION PROCESS
F
S11
SUPPLY A CONDENSED LIQUID TO A MICROTUBE
S12
SUPPLY THE REAGENT TO THE MICROTUBE
S13
PERFORM DNA STAINING AND RNA PROCESS
S14
SEND THE MEASUREMENT SAMPLE TO A DETECTION UNIT
B
C
S15
NO
IS A SHUTDOWN SIGNAL RECEIVED?
YES
S16
EXECUTE SHUTDOWN
END

FIG. 17

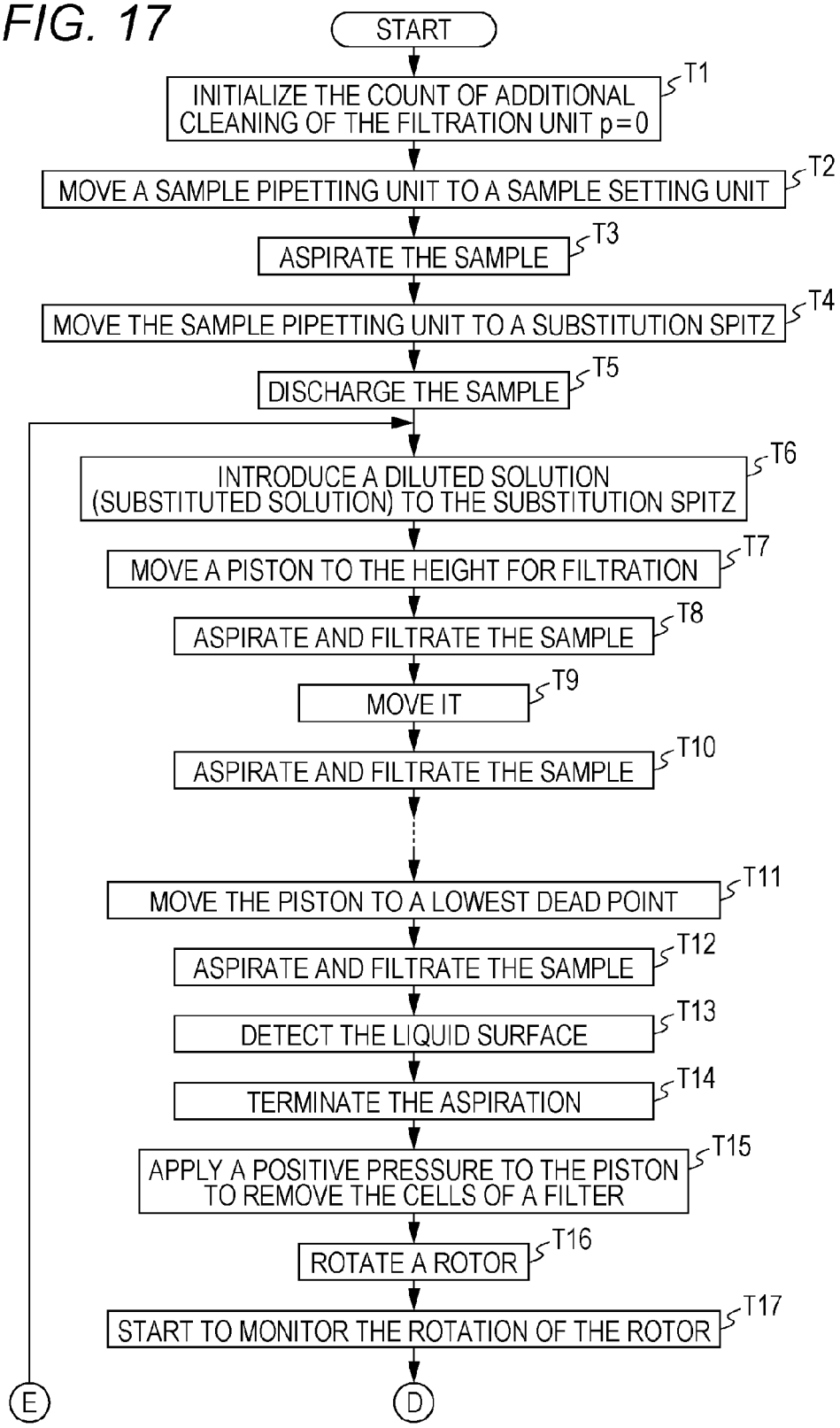

START
INITIALIZE THE COUNT OF ADDITIONAL CLEANING OF THE FILTRATION UNIT p=0
T1
MOVE A SAMPLE PIPETTING UNIT TO A SAMPLE SETTING UNIT
T2
ASPIRATE THE SAMPLE
T3
MOVE THE SAMPLE PIPETTING UNIT TO A SUBSTITUTION SPITZ
T4
DISCHARGE THE SAMPLE
T5
INTRODUCE A DILUTED SOLUTION (SUBSTITUTED SOLUTION) TO THE SUBSTITUTION SPITZ
T6
MOVE A PISTON TO THE HEIGHT FOR FILTRATION
T7
ASPIRATE AND FILTRATE THE SAMPLE
T8
MOVE IT
T9
ASPIRATE AND FILTRATE THE SAMPLE
T10
MOVE THE PISTON TO A LOWEST DEAD POINT
T11
ASPIRATE AND FILTRATE THE SAMPLE
T12
DETECT THE LIQUID SURFACE
T13
TERMINATE THE ASPIRATION
T14
APPLY A POSITIVE PRESSURE TO THE PISTON TO REMOVE THE CELLS OF A FILTER
T15
ROTATE A ROTOR
T16
START TO MONITOR THE ROTATION OF THE ROTOR
T17
E
D

FIG. 18

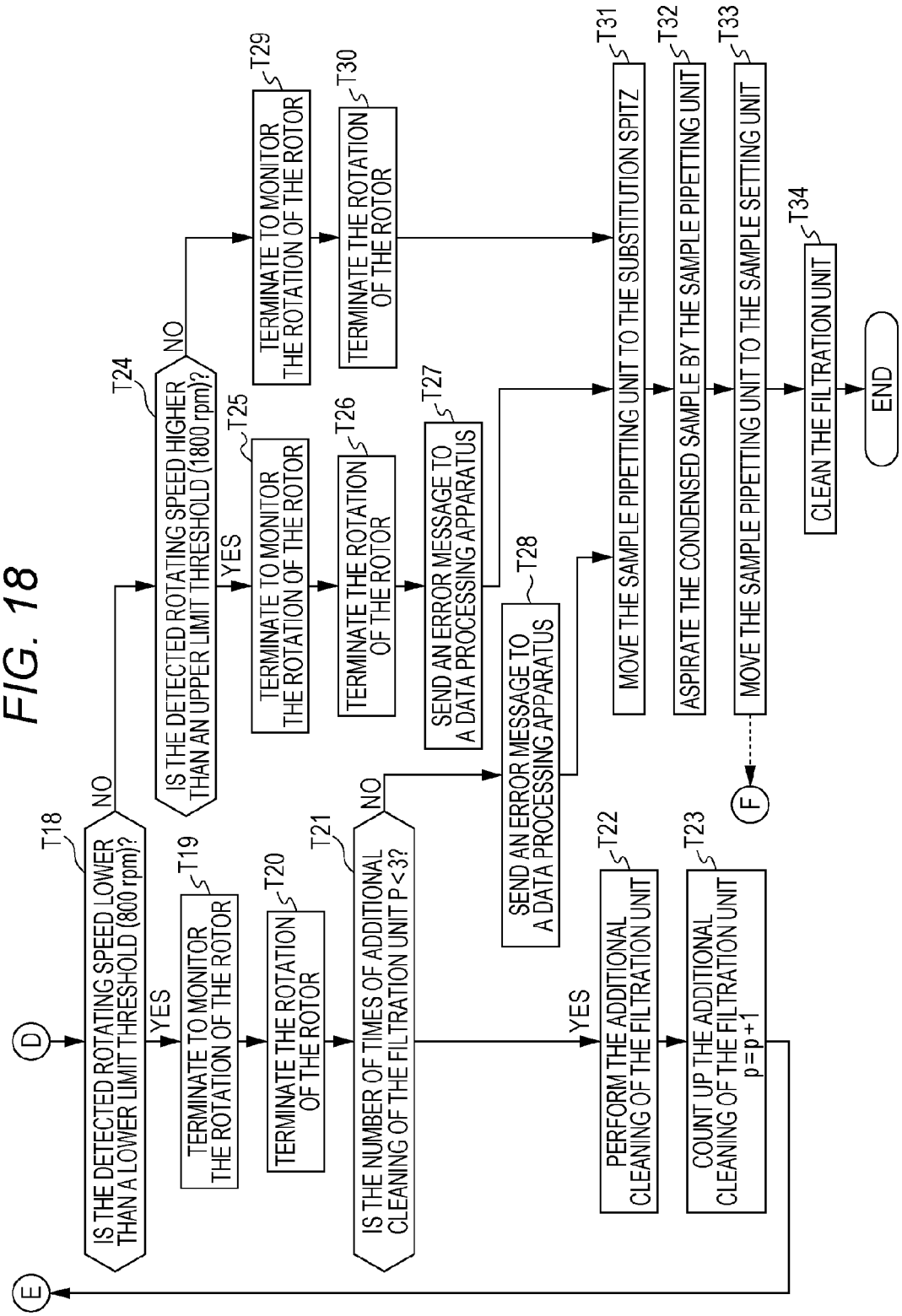

D
E
F
T18
IS THE DETECTED ROTATING SPEED LOWER THAN A LOWER LIMIT THRESHOLD (800 rpm)?
NO
YES
T19
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T20
TERMINATE THE ROTATION OF THE ROTOR
T21
IS THE NUMBER OF TIMES OF ADDITIONAL CLEANING OF THE FILTRATION UNIT P<3?
NO
YES
T22
PERFORM THE ADDITIONAL CLEANING OF THE FILTRATION UNIT
T23
COUNT UP THE ADDITIONAL CLEANING OF THE FILTRATION UNIT p=p+1
T24
IS THE DETECTED ROTATING SPEED HIGHER THAN AN UPPER LIMIT THRESHOLD (1800 rpm)?
NO
YES
T25
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T26
TERMINATE THE ROTATION OF THE ROTOR
T27
SEND AN ERROR MESSAGE TO A DATA PROCESSING APPARATUS
T28
SEND AN ERROR MESSAGE TO A DATA PROCESSING APPARATUS
T29
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T30
TERMINATE THE ROTATION OF THE ROTOR
T31
MOVE THE SAMPLE PIPETTING UNIT TO THE SUBSTITUTION SPITZ
T32
ASPIRATE THE CONDENSED SAMPLE BY THE SAMPLE PIPETTING UNIT
T33
MOVE THE SAMPLE PIPETTING UNIT TO THE SAMPLE SETTING UNIT
T34
CLEAN THE FILTRATION UNIT
END

FIG. 19

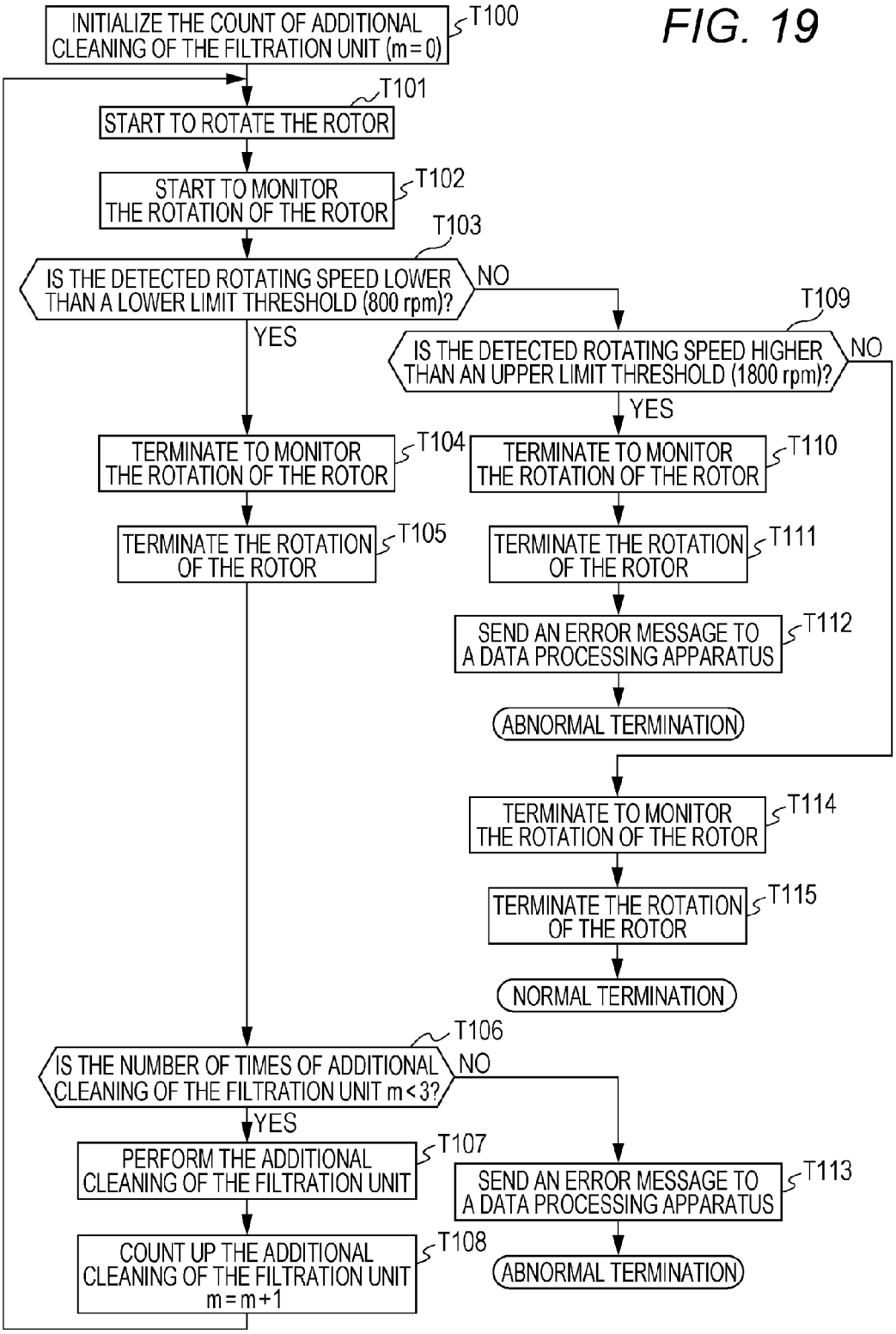
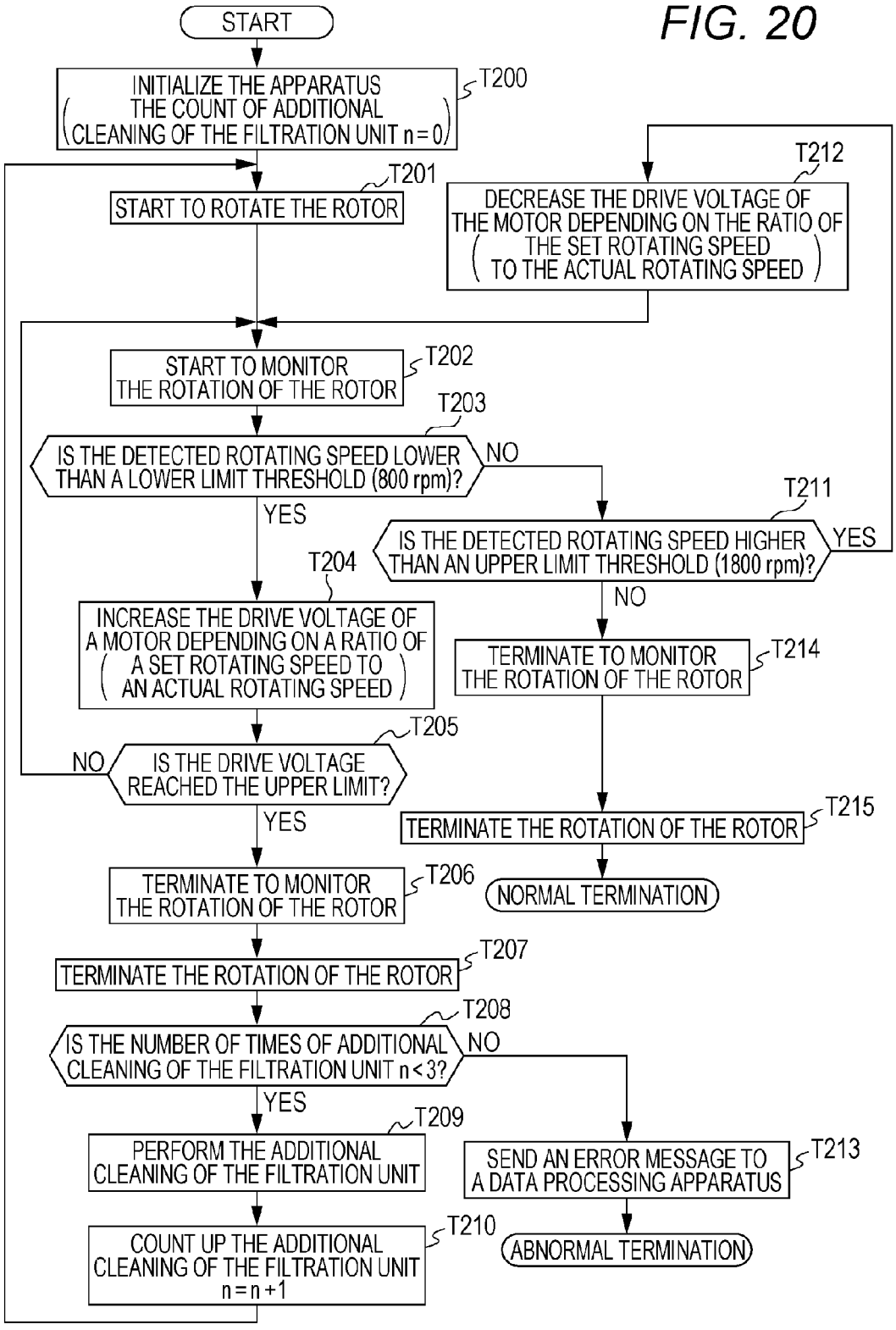

INITIALIZE THE COUNT OF ADDITIONAL CLEANING OF THE FILTRATION UNIT (m=0)
T100
START TO ROTATE THE ROTOR
T101
START TO MONITOR THE ROTATION OF THE ROTOR
T102
IS THE DETECTED ROTATING SPEED LOWER THAN A LOWER LIMIT THRESHOLD (800 rpm)?
T103
NO
YES
IS THE DETECTED ROTATING SPEED HIGHER THAN AN UPPER LIMIT THRESHOLD (1800 rpm)?
T109
NO
YES
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T104
TERMINATE THE ROTATION OF THE ROTOR
T105
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T110
TERMINATE THE ROTATION OF THE ROTOR
T111
SEND AN ERROR MESSAGE TO A DATA PROCESSING APPARATUS
T112
ABNORMAL TERMINATION
TERMINATE TO MONITOR THE ROTATION OF THE ROTOR
T114
TERMINATE THE ROTATION OF THE ROTOR
T115
NORMAL TERMINATION
IS THE NUMBER OF TIMES OF ADDITIONAL CLEANING OF THE FILTRATION UNIT m<3?
T106
NO
YES
PERFORM THE ADDITIONAL CLEANING OF THE FILTRATION UNIT
T107
SEND AN ERROR MESSAGE TO A DATA PROCESSING APPARATUS
T113
COUNT UP THE ADDITIONAL CLEANING OF THE FILTRATION UNIT m=m+1
T108
ABNORMAL TERMINATION

FIG. 20


START
INITIALIZE THE APPARATUS
THE COUNT OF ADDITIONAL
CLEANING OF THE FILTRATION UNIT n = 0
T200
START TO ROTATE THE ROTOR
T201
START TO MONITOR
THE ROTATION OF THE ROTOR
T202
IS THE DETECTED ROTATING SPEED LOWER
THAN A LOWER LIMIT THRESHOLD (800 rpm)?
T203
NO
YES
INCREASE THE DRIVE VOLTAGE OF
A MOTOR DEPENDING ON A RATIO OF
A SET ROTATING SPEED TO
AN ACTUAL ROTATING SPEED
T204
IS THE DRIVE VOLTAGE
REACHED THE UPPER LIMIT?
T205
NO
YES
TERMINATE TO MONITOR
THE ROTATION OF THE ROTOR
T206
TERMINATE THE ROTATION OF THE ROTOR
T207
IS THE NUMBER OF TIMES OF ADDITIONAL
CLEANING OF THE FILTRATION UNIT n < 3?
T208
NO
YES
PERFORM THE ADDITIONAL
CLEANING OF THE FILTRATION UNIT
T209
COUNT UP THE ADDITIONAL
CLEANING OF THE FILTRATION UNIT
n = n + 1
T210
DECREASE THE DRIVE VOLTAGE OF
THE MOTOR DEPENDING ON THE RATIO OF
THE SET ROTATING SPEED
TO THE ACTUAL ROTATING SPEED
T212
IS THE DETECTED ROTATING SPEED HIGHER
THAN AN UPPER LIMIT THRESHOLD (1800 rpm)?
T211
YES
NO
TERMINATE TO MONITOR
THE ROTATION OF THE ROTOR
T214
TERMINATE THE ROTATION OF THE ROTOR
T215
NORMAL TERMINATION
SEND AN ERROR MESSAGE TO
A DATA PROCESSING APPARATUS
T213
ABNORMAL TERMINATION

SAMPLE PREPARATION APPARATUS

FIELD OF THE INVENTION

The present invention relates to a sample preparation apparatus, a sample preparation method, and a computer program.

BACKGROUND

As a cell analyzer for analyzing cells contained in a biological sample collected from a living body, a cell analyzer for measuring epithelial cells of the uterine cervix contained a sample collected from the uterine cervix of a subject by a flow cytometer and screening cancer and atypical cells is conventionally known (e.g. European Patent publication No. EP2261632).

In addition to the epithelial cells to be analyzed, contaminants such as red blood cells and white blood cells are also contained in the sample collected from the uterine cervix of the subject. When such a sample is measured as it is, the presence of the contaminants affects the measured results, resulting in being unable to perform an accurate screening. Therefore, it is necessary to discriminate the epithelial cells to be analyzed from the contaminants.

In the apparatus described in European Patent publication No. EP2261632, the epithelial cells are discriminated from the contaminants by trapping the epithelial cells to be analyzed in a filter, aspirating the contaminants passed the filter, and discharging them using the fact that the size of the epithelial cells to be analyzed is larger than that of the contaminants.

In order to prepare a measurement sample containing the epithelial cells, it is necessary to detach the epithelial cells trapped in the filter from the filter and recover them. The detachment is performed by applying a shearing force generated by rotating a rotor arranged adjacent to the filtration surface of the filter to the surface of the filter.

In the cell analyzer described in European Patent publication No. EP2261632, when detaching the epithelial cells attached to the filter by the rotor, the rotor may not rotate or the rotation may not be sufficient due to reasons that the epithelial cells are adhered to the rotor or the wall surface around the rotor. When the rotation of the rotor is not sufficient, the epithelial cells to be measured cannot be sufficiently taken.

SUMMARY

The scope of the present invention is defined solely by the appended claims, and is not affected to any degree by the statements within this summary.

A first aspect of the present invention is a sample preparation apparatus comprising: a filter which separates predetermined cells from a liquid sample containing a plurality types of cells; a rotor which includes a magnetic body and detaches the predetermined cells attached to the filter by rotation; a driving unit which rotates the rotor using a magnetic force; and a rotation information acquiring unit which acquires a rotation information of the rotor when the driving unit rotates the rotor.

A second aspect of the present invention is a sample preparation method, comprising: acquiring the rotation information of the rotor, wherein the rotor detaches predetermined cells attached to the filter which separates the predetermined cells from the liquid sample containing the plurality types of cells and which includes the magnetic body; and controlling the driving unit which rotates the rotor using the magnetic force based on the acquired rotation information of the rotor.

A third aspect of the present invention is a computer program product, comprising: a computer readable medium; and instructions, on the computer readable medium, adapted to enable a general purpose computer to perform operations, comprising: acquiring the rotation information of the rotor, wherein the rotor detaches predetermined cells attached to the filter which separates the predetermined cells from the liquid sample containing the plurality types of cells and which includes the magnetic body; and controlling the driving unit which rotates the rotor using the magnetic force based on the acquired rotation information of the rotor.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a perspective view of a cell analyzer having a sample preparation apparatus according to one embodiment of the present invention;

FIG. **2** is a block diagram showing an internal configuration of a measurement apparatus;

FIG. **3** is a block diagram showing an internal configuration of the sample preparation apparatus;

FIG. **4** is a block diagram showing an internal configuration of a data processing apparatus;

FIG. **5** is a functional block diagram of a flow cytometer which includes a detection unit;

FIG. **6** is a side view showing an optical system of the flow cytometer;

FIG. **7** is a fluid circuit diagram of a preparation device unit;

FIG. **8** is a fluid circuit diagram of the preparation device unit;

FIG. **9** is a cross sectional explanatory view of a substitution container;

FIG. **10** is a perspective explanatory diagram of a rotor;

FIG. **11**A is a plan view of the rotor shown in FIG. **10** and FIG. **11**B is a side view of the rotor shown in FIG. **10**;

FIG. **12** is a perspective explanatory diagram of a light emitting unit and a light receiving unit;

FIG. **13** is an explanatory diagram of an example of a condensed sample holding chamber;

FIG. **14** is a pattern diagram showing a process for concentrating analytes in a discrimination/substitution unit;

FIG. **15** is a flow chart showing processes which are performed by each control unit of the cell analyzer;

FIG. **16** is a flow chart showing processes which are performed by each control unit of the cell analyzer;

FIG. **17** is a flow chart showing a discrimination/substitution process;

FIG. **18** is a flow chart showing a discrimination/substitution process;

FIG. **19** is a flow chart for checking the rotation after the measurement; and

FIG. **20** is a flow chart for checking the rotation at the time of activating the apparatus.

DETAILED DESCRIPTION OF THE EMBODIMENT

The embodiments of the sample preparation apparatus of the present invention will be described in detail below with reference to the accompanying drawings.

The sample preparation apparatus of the present invention can be used in the cell analyzer which analyzes cells collected from patients. First, the cell analyzer will be described.

[Overall Configuration of the Cell Analyzer]

FIG. **1** is a perspective view of a cell analyzer **1** having a sample preparation apparatus according to one embodiment of the present invention.

The cell analyzer **1** is used for determining whether or not cancer cells are contained in the cells by flowing a measurement sample containing the cells collected from the patients into a flow cell, irradiating the measurement sample flowing through the flow cell with a laser beam, detecting light from the measurement sample (scattered light or fluorescence (e.g. forward scattered light and lateral fluorescence)), and analyzing the light signals thereof.

More specifically, the cell analyzer **1** of the present embodiment is intended to analyze epithelial cells of the uterine cervix and used for screening uterine cervix carcinoma.

As shown in FIG. **1**, the cell analyzer **1** includes a measurement apparatus **2** which performs optical measurement with a laser beam on the measurement sample, a sample preparation apparatus **3** which produces the measurement sample to be supplied to the measurement apparatus **2** by subjecting a biological sample collected from a subject to pretreatments such as cleaning and staining, and a data processing apparatus **4** which analyzes the measured results in the measurement apparatus **2**.

A main constituent element of the cell analyzer **1** will be sequentially described.

[Internal Configuration of the Measurement Apparatus]

FIG. **2** is a block diagram showing an internal configuration of a measurement apparatus **2**.

As shown in FIG. **2**, the measurement apparatus **2** includes a detection unit **6**, a signal processing unit **7**, a measurement control unit **8**, and an I/O interface **9**.

Among them, the detection unit **6** detects cells to be measured and the number and size of nuclei in the cells from the measurement sample and a flow cytometer **10** shown in FIGS. **5** and **6** is employed in the present embodiment.

The signal processing unit **7** includes a signal processing circuit which performs a required signal process on an output signal from the detection unit **6**. The measurement control unit **8** includes a microprocessor **11** and a memory unit **12** and the memory unit **12** includes a ROM, a RAM, and the like.

Control programs which perform operation control of the detection unit **6** or the signal processing unit **7** as well as data required for executing the control programs are stored in the ROM of the memory unit **12**. The microprocessor **11** is capable of executing the control programs loaded in the RAM or directly executing the control programs in the ROM.

The microprocessor **11** of the measurement control unit **8** is connected to the data processing apparatus **4** and a microprocessor **19** of a preparation control unit **16** to be described later through the I/O interface **9**. Thus, the data processing apparatus **4** can transmit and receive data processed by the microprocessor itself or data required for the microprocessor's own process with the microprocessor **19** of the preparation control unit **16**.

[Internal Configuration of the Sample Preparation Apparatus]

FIG. **3** is a block diagram showing an internal configuration of the sample preparation apparatus **3**.

As shown in FIG. **3**, the sample preparation apparatus **3** includes the preparation control unit **16**, an I/O interface **17**, and a preparation device unit **18** which automatically adjusts components of the biological sample.

The preparation control unit **16** includes the microprocessor **19**, a memory unit **20**, a sensor driver **21**, and a driving unit driver **22**. The memory unit **20** includes a ROM, a RAM, and the like.

The preparation device unit **18** of the present embodiment is configured by a sample setting unit **24**, a cell dispersion unit **25**, a sample pipetting unit **26**, a sample quantitating unit **27**, a reagent quantitating unit **28**, and a discrimination/substitution unit **29**.

A plurality of biological sample containers **53** and measurement sample containers **54** which hold biological samples collected from the patients and a preservative solution containing methanol as a main ingredient (see FIG. **7**) are set in the sample setting unit **24** among them. The cell dispersion unit **25** forcedly disperses cells contained in the sample by stirring a mixed solution of the biological samples and the preservative solution in the biological sample containers **53**.

The sample pipetting unit **26** introduces the mixed solution of the biological samples containing the dispersed cells and the preservative solution retrieved from the biological sample containers **53** into the fluid circuit of the preparation device unit **18**, and retrieves a prepared liquid sample returned to the measurement sample containers **54** from the measurement sample containers **54**. The sample quantitating unit **27** quantifies the mixed solution of the biological samples and the preservative solution to be supplied to the fluid circuit. The reagent quantitating unit **28** quantifies a reagent such as a stain solution to be added to the biological samples.

The discrimination/substitution unit **29** substitutes the preservative solution with a diluted solution and discriminates cells to be measured from the other cells (red blood cells, white blood cells, etc.) and bacteria, and the like. The discrimination/substitution unit **29** prepares a liquid sample in which the concentration of the cells to be measured is increased from the liquid sample containing the discriminated and substituted cells to be measured. The configuration of the fluid circuit of the preparation device unit **18** having respective units **24** to **29** (FIGS. **7** to **8**) will be described later.

Control programs which perform operation control of the sensor driver **21** and the driving unit driver **22** as well as data required for executing the control programs are stored in the ROM of the memory unit **20**. The microprocessor **19** is capable of executing the control programs loaded in the RAM or directly executing the control programs in the ROM.

The microprocessor **19** of the preparation control unit **16** is connected to the microprocessor **11** of the measurement control unit **8** through the I/O interface **17**. Thus, the microprocessor **19** can transmit and receive data processed by the microprocessor itself or data required for the microprocessor's own process with the microprocessor **11** of the measurement control unit **8**.

The microprocessor **19** of the preparation control unit **16** is connected to sensors of respective units **24** to **29** in the preparation device unit **18** and a driving motor configured by the driving unit through the sensor driver **21** and a driving unit driver **22**, executes the control programs based on detection signals from the sensors, and controls the operation of the driving unit.

[Internal Configuration of the Data Processing Unit]

FIG. **4** is a block diagram showing an internal configuration of a data processing apparatus **4**.

As shown in FIG. **4**, the data processing apparatus **4** of the present embodiment is configured by a personal computer, for example, a notebook PC (a desktop type PC may be used.) and mainly includes a processing body **31**, a display **32**, and an input unit **33**.

The processing body **31** includes a CPU **34**, a ROM **35**, a RAM **36**, a hard disk **37**, a read-out device **38**, an I/O interface **39**, and an image output interface **40**. Each of these units is communicably connected by an internal bus.

The CPU **34** is capable of executing the computer programs stored in the ROM **35** and the computer programs loaded in the RAM **36**.

The ROM **35** is configured by a mask ROM, a PROM, an EPROM, an EEPROM, and the like. The computer programs to be executed by CPU **34** and data to be used for the computer programs are stored in the ROM **35**.

The RAM **36** is configured by a SRAM, a DRAM, or the like, and is used to read out various computer programs recorded on the ROM **35** and the hard disk **37** or is used as a work region of the CPU **34** when executing the computer programs.

Various computer programs to be executed by the CPU **34** such as operating system and application program, as well as data used in executing the programs are installed in the hard disk **37**.

An operating system providing a graphical user interface environment such as Windows (registered trademark) manufactured and sold by US Microsoft Co. is installed in the hard disc **37**.

Further, an operation program **41** which performs transmission of operation instructions to the measurement control unit **8** and the preparation control unit **16**, processes of receiving and analyzing measured results performed by the measurement apparatus **2**, and display of processed analysis results is installed in the hard disc **37**. The operation program **41** is assumed to operate on the operating system.

The read-out device **38** is configured by a flexible disk drive, a CD-ROM drive or a DVD-ROM drive. The read-out device **38** is capable of reading out computer programs or data recorded in a portable recording medium.

For example, the input/output interface **39** is configured by a serial interface such as USB, IEEE 1394, and RS-232C, a parallel interface such as SCSI, IDE, and IEEE 1284, and an analog interface including D/A and ND converters.

The input/output interface **39** is connected to the input device **33** including a keyboard and a mouse. The user can input data to the computer using the input unit **33**.

The input/output interface **39** is also connected to the I/O interface **9** of the measurement apparatus **2**. Thus, the measurement apparatus **2** can transmit and receive data with the data processing apparatus **4**.

The image output interface **40** is connected to the display **32** including a LCD or a CRT. The image output interface **40** allows the display **32** to output an image signal corresponding to the image data from the CPU **34**.

[Configuration of the Detection Unit (Flow Cytometer)]

FIG. **5** is a functional block diagram of the flow cytometer **10** which includes the detection unit **6**. FIG. **6** is a side view showing an optical system of the flow cytometer **10** which includes the detection unit **6**.

As shown in FIG. **5**, a lens system **43** of the flow cytometer **10** focuses the laser beam from a semiconductor laser **44** which is a light source on the measurement sample flowing through a flow cell **45**. A light collecting lens **46** focuses the forward scattered light of the cells in the measurement sample on a scattered light detector including a photodiode **47**.

The lens system **43** is illustrated as a single lens in FIG. **5**. Specifically, it has, for example, a configuration shown in FIG. **6**.

That is, the lens system **43** of the present embodiment is configured by a collimator lens **43***a*, a cylindrical lens system (a planoconvex cylindrical lens **43***b*+a biconcave cylindrical lens **43***c*), and a condenser lens system (a condenser lens **43***d*+a condenser lens **43***e*) in this order from the side of the semiconductor laser **44** (the left-hand side of FIG. **6**).

Returning to FIG. **5**, a lateral light collecting lens **48** focuses the lateral scattered light and the lateral fluorescence of cells to be measured or nuclei in the cells on a dichroic mirror **49**. The dichroic mirror **49** reflects the lateral scattered light on a photomultiplier **50** which is a scattered light detector and transmits the lateral fluorescence to a photomultiplier **51** which is a fluorescence detector. These lights reflect features of the cells and nuclei in the measurement sample.

The photodiode **47** and each of the photomultipliers **50** and **51** convert received light signals into electric signals and output a forward scattered light signal (FSC), a lateral scattered light signal (SSC), and a lateral fluorescence signal (SFL), respectively. These output signals are amplified by a preamplifier (not shown) and sent to the signal processing unit **7** (see FIG. **2**) of the measurement apparatus **2**.

Each of the signals FSC, SSC, and SFL processed by the signal processing unit **7** of the measurement apparatus **2** is transmitted to the data processing apparatus **4** from the I/O interface **9** by the microprocessor **11**.

The CPU **34** of the data processing apparatus **4** (see FIG. **4**) creates a scattergram for analyzing the cells and nuclei from each of the signals FSC, SSC, and SFL by executing the operation program **41** and determines whether or not the cells in the measurement sample are abnormal cells, specifically cancerous cells based on the scattergram.

An average size of epithelial cells of the uterine cervix is about 60 μm. The size of nuclei of the epithelial cells of the uterine cervix is from 5 to 7 μm. When the cells become cancerous, the frequency of cell division is abnormally increased and the size of nuclei becomes from 10 to 15 μm. Thus, a N/C ratio (size of nuclei/size of cells) is higher than that of normal cells.

Therefore, there is provided an index for determining whether or not the cells become cancerous by detecting the size of cells and nuclei.

In the present embodiment, the photodiode **47** detects the scattered light from the measurement sample flowing through the flow cell **45** and the photomultiplier **51** detects the fluorescence from the measurement sample flowing through the flow cell **45**.

The signal processing unit **7** of the measurement apparatus **2** acquires a pulse width of the scattered light signal which is a value reflecting the size of the cells to be measured from the scattered light signal output from the photodiode **47** and acquires a pulse width of the fluorescence signal which is a value reflecting the size of nuclei of the cells to be measured from the fluorescence signal output the photomultiplier **51**.

The CPU **34** of the data processing apparatus **4** which includes an analyzing unit is configured to determine whether or not the cells to be measured are abnormal cells based on the value reflecting the size of the cells to be measured and the value reflecting the size of nuclei of the cells to be measured acquired by the signal processing unit **7**.

Specifically, the CPU **34** of the data processing apparatus **4** determines that the cells to be measured are abnormal cells when the peak, nuclear diameter, and area values of the cells to be measured are larger than a predetermined threshold.

[Fluid Circuit of the Preparation Device Unit]

FIG. **7** is a fluid circuit diagram of the sample setting unit **24** of the preparation device unit **18**, the cell dispersion unit **25**, the sample pipetting unit **26**, the sample quantitating unit **27**, and the reagent quantitating unit **28**. FIG. **8** is a fluid circuit diagram of the discrimination/substitution unit **29** of the preparation device unit **18**.

As shown in FIG. **7**, the sample setting unit **24** includes a circular rotatable table **24**A and a driving unit **24**B which rotates and drives the circular rotatable table **24**A. The driving unit **24**B includes a stepping motor. A holder capable of setting the biological sample containers **53** which hold the mixed solution of the biological samples and the preservative solution and the measurement sample containers **54** which hold the liquid sample prepared by the discrimination/substitution unit **29** in which the concentration of the cells to be measured is increased is provided in the outer periphery part of the rotating table **24**A.

The cell dispersion unit **25** includes a stirring rod **25**A which stirs the mixed solution of the biological samples and the preservative solution in the biological sample containers **53** and a driving unit **25**B which rotates and drives the stirring rod **25**A. The driving unit **25**B including a DC motor inserts the stirring rod **25**A into the biological sample containers **53** and rotates them. Thus, the mixed solution in the biological sample containers **53** is stirred and thereby the cells contained in the biological samples can be dispersed.

The sample pipetting unit **26** includes a first pipette **26**A and a second pipette **26**B. The first pipette **26**A aspirates the mixed solution of the biological samples and the preservative solution in the biological sample containers **53**, moves to a substitution container **57** of the discrimination/substitution unit **29** shown in FIG. **8**, and discharges the mixed solution to the substitution container **57**. The mixed solution discharged to the substitution container **57** is discriminated and substituted, and a liquid sample in which the concentration of the cells to be measured is increased is prepared from the discriminated and substituted liquid sample containing the cells to be measured. Thereafter, the first pipette **26**A aspirates the liquid sample in which the concentration of the cells to be measured is increased from the substitution container **57**, moves to the measurement sample container **54** arranged in the sample setting unit **24** of FIG. **7**, and discharges the liquid sample to the measurement sample container **54**. The second pipette **26**B discharges a reagent such as a stain solution which is supplied from the reagent quantitating unit **28** to the measurement sample container **54**.

The sample quantitating unit **27** includes a quantitative cylinder **27**A and a driving unit **27**B including a stepping motor which moves a quantitative piston inserted into the cylinder **27**A up and down. The quantitative cylinder **27**A is connected to the first pipette **26**A through a duct via a direction switching valve V**1**.

As shown in FIG. **8**, the discrimination/substitution unit **29** includes the substitution container **57** having an upwardly opened shape, a piston **58** movable in the substitution container **57** in the up and down direction, and a driving unit **59** including a stepping motor which moves the piston **58** up and down in the substitution container **57**.

The substitution container **57** is connected to a cleaning fluid unit **90** through a duct via switching valves V**4** and V**5**. A cleaning fluid is supplied from the cleaning fluid unit **90** to the substitution container **57** via the switching valves V**4** and V**5**. Further, the substitution container **57** is connected to a diluting fluid unit **55** through a duct via a switching valve V**6**. A diluting fluid is supplied from the diluting fluid unit **55** to the substitution container **57** via the switching valve V**6**.

The piston **58** includes a hollow cylinder including a filter **60** which does not pass the cells to be measured (epithelial cells) and passes cells having a diameter smaller than that of the cells to be measured (red blood cells, white blood cells, etc.) at the lower part. The piston **58** is connected to a positive pressure source **71** through a duct via a switching valve V**8**. Thus, a positive pressure can be supplied to the inside of the piston **58** by opening the switching valve V**8**. The internal space of the piston **58** is connected to the outside via a switching valve V**9**. The internal space of the piston **58** can be opened to the atmosphere by opening the switching valve V**9**.

The piston **58** is connected to a discarding unit **61** of filtrate through a duct via switching valves V**10** and V**12**. Thus, a filtrate aspirated from the inside of the piston **58** is discarded to the outside through the switching valves V**10** and V**12**.

The piston **58** is connected to the cleaning fluid unit **90** through a duct via a switching valve V**7**. The cleaning fluid supplied from the cleaning fluid unit **90** is used for cleaning the piston **58** and the substitution container **57**. The cleaning fluid which has cleaned the piston **58** and the inside of the substitution container **57** is discharged to the discarding unit **61** via switching valves V**11** and V**13**.

Returning to FIG. **7**, the reagent quantitating unit **28** includes a pair of quantitative cylinders **28**A and **28**B and a driving unit **28**C including a stepping motor which moves quantitative pistons inserted into each of the cylinders **28**A and **28**B, respectively up and down. Each of the quantitative cylinders **28**A and **28**B is connected to the second pipette **26**B through a duct via supply switching valves V**2** and V**3**, respectively. A reagent quantified by each of the quantitative cylinders **28**A and **28**B is supplied to the second pipette **26**B via the supply switching valves V**2** and V**3** and discharged to the measurement sample container **54**.

Thus, the liquid sample in which the concentration of the cells to be measured is increased, being held in the measurement sample container **54** of the sample setting unit **24**, can be mixed with a plurality types of reagents quantified by the quantitating unit **28** in a predetermined amount.

In the present embodiment, there are two types of reagents to be quantified by each of the quantitative cylinders **28**A and **28**B of the reagent quantitating unit **28**. The reagent to be added to the biological samples after weighting it by the quantitative cylinder **28**A is a dye solution for performing PI staining. The reagent to be added to the biological samples after weighting it by the other quantitative cylinder **28**B is RNase for subjecting cells to an RNA process. The PI staining is performed with propidium iodide (PI) which is a fluorescent staining solution containing a pigment. Since nuclei are selectively stained in the PI staining, the fluorescence from the nuclei can be detected. The RNA process is a process of melting RNA in cells. Since the dye solution stains both RNA and DNA of epithelial cells, RNA is melted by performing the RNA process and is not stained by the dye solution. Therefore, the DNA of a cell nucleus can be accurately measured.

The operation control of the driving units and the switching valves (electromagnetic valves) V**1** to V**13** in each unit shown in FIGS. **7** and **8** is performed based on a control command from the preparation control unit **16** (microprocessor **19**).

[Configuration of the Discrimination/Substitution Unit]

The configuration of the discrimination/substitution unit **29** in the present embodiment will be described with reference to FIG. **9**. FIG. **9** is a cross sectional explanatory view of the substitution container **57** in the discrimination/substitution unit **29** of FIG. **8** in the present embodiment.

As shown in FIG. **9**, the discrimination/substitution unit **29** of the present embodiment includes the substitution container **57**, the piston **58** made of a cylindrical body movable in the substitution container **57** in the up and down direction, a filter **60** for sorting the cells to be measured which is arranged at the lower part of the piston **58** made of a cylindrical body, and a liquid surface detection sensor **82** which detects the surface of the liquid containing the cells to be measured. The discrimination/substitution unit **29** detaches the cells to be measured which has been trapped by the filter **60** from the filter **60** and

includes the filter **60**, a rotor **72** which is a rotor, a driving unit (magnetic stirrer) **70** which rotates the rotor **72** with a magnetic force, and a rotation information acquiring unit **100** which acquires rotation information of the rotor **72**. The driving unit **70** includes a magnet **69** which adsorbs to the rotor **72** with the magnetic force and a driving motor **70***a* which rotates the magnet **69**. The rotation information acquiring unit **100** includes a light emitting unit **101**, a light receiving unit **102**, a signal level comparator **105**, and a counter unit **106**. The driving unit (magnetic stirrer) **70** is not particularly limited as long as it rotates the rotor **72** with the magnetic force. For example, known magnetic stirrers can be used.

The substitution container **57** includes a holding chamber **68** which can hold analytes to be analyzed (the cells to be measured) and a condensed sample holding chamber **80** which is communicated with and arranged in the holding chamber. The rotor **72** which moves the cells to be measured contained in the liquid sample from the holding chamber **68** to the condensed sample holding chamber **80** and allows the cells to be measured which has been trapped on the lower surface of the filter **60** to be detached by a shearing force due to rotation is held in the holding chamber **68**. The rotor **72** is configured to be rotated by the magnetic force. The magnet **69** for providing the magnetic force to the rotor **72** and the driving motor **70***a* which is a driving unit for rotating the magnet **69** are provided on the lower side of the bottom of the holding chamber **68**.

The rotor **72** has a circular cylindrical shape and is made of polychloro-trifluoroethylene (PCTFE), and the like. FIG. **10** is a perspective explanatory diagram showing an example of the rotor **72** in the present embodiment. FIG. **11**A is a top view of the rotor **72** in FIG. **10** and FIG. **11**B is a side view of the rotor **72** in FIG. **10**.

A hole (concave portion) **73** facing the center is formed in the peripheral surface of the rotor **72**. A magnet **75** having a round bar shape and a light reflecting unit **103** having a cylindrical shape made of stainless steel are contained in the hole **73**. The magnet **69** is rotated by the driving motor **70***a*, whereby the rotor **72** including the magnet **75** to which the magnetic force is applied from the magnet **69** rotates. An end surface **103***a* of the light reflecting unit **103** is exposed to the outside and is provided so that the light emitted from the light emitting unit **101** is reflected thereon. The end surface **103***a* is ground to improve light reflectivity.

In the present embodiment, the magnet **75** has been used to rotate the rotor **72** with the magnetic force generated from the magnetic stirrer **70**, however, it is not particularly limited as long as it is a substance having magnetism. Preferably, it is a substance having ferromagnetism (ferromagnetic body). Examples of the ferromagnetic body include a neodymium magnet, a samarium-cobalt magnet, a ferrite magnet, an iron-platinum magnet, an iron-chromium-cobalt magnet, and an alnico magnet.

Two ribs **74** which cross each other are formed on the upper surface of the rotor **72**. The ribs **74** are extended to the peripheral edge. The stirring efficiency of the liquid sample present between the lower surface of the filter **60** and the upper surface of the rotor **72** can be improved by forming the ribs **74**. As a result, the cells to be measured attached to the lower surface of the filter **60** can be effectively detached from the filter **60**. The movement of the cells to be measured to the condensed sample holding chamber to be described later can be performed effectively. The projection height of the ribs **74** is not particularly limited in the present invention, and it is from about 0.3 to 1.0 mm as an indication.

The distance between the lower surface (filtration surface) of the filter **60** and the upper surface of the ribs **74** of the rotor **72** facing the lower surface is not particularly limited and it is preferably 1 mm or less, more preferably 0.6 mm or less. The rotating speed of the magnet **69** which rotates the rotor **72**, namely the rotating speed of the driving motor **70***a* is set preferably to the range of 1000 to 2000 rpm, more preferably to about 1300 rpm.

Returning to FIG. **9**, the filter **60** is arranged on the bottom of the piston **58** through a holding fixture **65**. The piston **58** serves as a liquid separating unit which separates a liquid into a first liquid which mainly contains the cells to be measured and a second liquid which mainly contains cells having a diameter smaller than that of the cells to be measured by passing the liquid through the filter **60**.

In the present embodiment, epithelial cells of the uterine cervix are assumed as the cells to be measured. The size of the epithelial cells is from about 20 to 80 μm (the average size is about 60 μm). The size of red blood cells which are cells smaller than the cells to be measured is from about 7 to 10 μm. Similarly, the size of white blood cells which are cells smaller than the cells to be measured is from about 8 to 15 μm. The size of contaminants such as bacteria is from about 1 to several μm.

Then, the filter **60** in the present embodiment is made of metal having through holes with a diameter smaller than 20 μm (a diameter of 8 to 20 μm) by Chemical Vapor Deposition (CVD) so that epithelial cells do not pass the through holes of the filter **60** even in a state where pressure is applied to the liquid in the substitution container **57** and do not move to the piston **58**. The through holes of the CVD filter made of metal have little deformation as compared with other filters made of resin and even a filter made of metal mesh, which is advantageous for improving an aperture ratio.

The pore diameter of the filter **60** has been set to the range of 8 to 20 (m, because many phenomena that the through holes are clogged with the cells and the contaminants at an early stage are observed when the pore diameter is less than 8 (m, and the epithelial cells pass the through holes more often in a state where pressure is applied to the liquid in the substitution container **57** when the pore diameter exceeds 20 (m. The pore diameter of the filter **60** is more preferably around 15 (m.

The liquid surface detection sensor **82** is arranged at the lower part of the substitution container **57** to detect the surface of the first liquid in the substitution container **57**. The liquid surface detection sensor **82** is a capacitance type sensor and the distal end of the liquid surface detection sensor **82** is projected from the inner surface of the substitution container **57** to the inner side by about 2 to 3 mm. A sensor unit **82***a* having a pin shape is provided on the distal end of the projected portion. The liquid surface detection sensor **82** is used to detect that the surface of the first liquid containing the cells to be measured has reached the position, nearly at the bottom of the filter **60**.

In the present embodiment, the sensor unit **82***a* is arranged at the upper side by about 2.0 mm relative to the lower surface of the filter **60** and the aspiration of the second liquid in the piston **58** is stopped after a lapse of predetermined time after the detection signal is received from the sensor unit **82***a* taking into consideration the influence of the surface tension and the aspiration rate of the second liquid. The sensor unit **82***a* having a pin shape is arranged at the obliquely upper side, whereby draining of the liquid can be improved and the accuracy of the liquid surface detection can be improved. In this case, an angle to arrange the sensor with respect to a horizontal surface is in the range of about 5 to 90 degrees.

In the present embodiment, the holding chamber **68** and the condensed sample holding chamber **80** communicated with

and arranged in the periphery part of the holding chamber **68** are arranged at the bottom of the substitution container **57** (see FIG. **13**). The condensed sample holding chamber **80** plays a role in collecting the cells to be measured which have been moved by the rotation of the rotor **72** held in the holding chamber **68**. Some of the cells to be measured are trapped and attached to the lower side of the filter **60** by discrimination process to be described later, however, the attached cells to be measured are torn from the lower surface of the filter **60** by the rotation of the rotor **72** and collected into the condensed sample holding chamber **80** communicated with and arranged in the periphery part of the holding chamber **68** by a centrifugal force generated by the rotation of the rotor **72**.

Returning to FIG. **9**, the rotation information acquiring unit **100** is provided to acquire the rotation information of the rotor **72**, specifically, the rotating speed per unit time in order to determine whether or not the rotor **72** is rotating. The rotation information acquiring unit **100** includes the light emitting unit **101** which irradiates the rotor **72** with light, the light receiving unit **102** which detects the light emitted from the light emitting unit **101**, the signal level comparator **105** which compares a signal level based on the light detected by the light receiving unit **102** with a reference level, and the counter unit **106** for counting the number of times exceeding the reference level and calculating the rotating speed of the rotor **72** by the signal.

The rotation information of the rotor **72** is acquired based on the number of times that the light receiving unit **102** has detected the light from the light emitting unit **101** reflected by the light reflecting unit **103**. Specifically, the light emitted from the light emitting unit **101** toward the rotor **72** rotating is reflected by the light reflecting unit **103** and detected by the light receiving unit **102** only when the light reflecting unit **103** provided in the peripheral surface of the rotor **72** faces the light emitting unit **101**. Thus, the rotating speed of the rotor **72** per unit time can be acquired based on the number of times that the light receiving unit **102** has detected the light per unit time.

FIG. **12** is a perspective explanatory diagram showing a configuration of the light emitting unit **101** and the light receiving unit **102**. The light emitting unit **101** and the light receiving unit **102** are arranged side by side. The light emitted from the light emitting unit **101** toward the rotor **72** is reflected by the light reflecting unit **103** and detected by the light receiving unit **102** only when the light emitting unit **101** faces the light reflecting unit **103** of the rotor **72**. The light emitting unit **101** uses an LED as a light source and is fixed to a supporting unit **104** arranged near the lower part of the substitution container **57** so as to irradiate the outer end surface of the light reflecting unit **103** provided in the peripheral surface of the rotor **72** arranged near the bottom of the substitution container **57** with LED light. The laser can also be used as a light source in place of the LED. Both the LED and the laser have a difference in detection distance. In the case of the laser beam, the detection distance is longer than that of the LED light. Thus, the detection accuracy can be improved and the design flexibility of the substitution container **57** can be improved. When the LED is used, the light emitting unit **101** can be produced in a small size at low cost.

In the present embodiment, the substitution container **57** is made of a vinyl chloride resin which is a light transmittable transparent synthetic resin using the LED as a light source. As shown in FIG. **9**, a wall thickness t of a portion to which the light is transmitted is set to, for example, 7.75 mm taking into consideration the detection distance. A distance d from the outer periphery surface of the substitution container **57** (almost the same as the light-irradiated surface of the light emitting unit **101**) to the outer end surface of the light reflecting unit **103** (light-reflected surface) is set to, for example, 8.00 mm.

The light reflected by the light reflecting unit **103** is detected by the light receiving unit **102**. A signal based on the reflected light from the light reflecting unit **103** which has been detected by the light receiving unit **102** is compared with a reference level by the signal level comparator **105** of the rotation information acquiring unit **100**. When the signal level is larger than the reference level, it is counted by the counter unit **106** by PLD, and the like. The rotating speed of the rotor **72** per unit time is calculated based on the resulting value. The rotating speed calculated by the counter unit **106** can be read by a control unit **107** including a CPU. When the rotating speed is lower than a predetermined value, a voltage control signal is supplied to a drive voltage control circuit **109** via a D/A converter **108**. A drive voltage of the driving motor **70***a* is increased so as to increase the rotating speed by the drive voltage control circuit **109** which has received the control signal. When the rotating speed is higher than the predetermined value, the voltage control signal is supplied to the drive voltage control circuit **109** via the D/A converter **108**. The drive voltage of the driving motor **70***a* is reduced so as to decrease the rotating speed by the drive voltage control circuit **109** which has received the control signal. Thus, in the present embodiment, the rotating speed of the rotor **72** can be feedback-controlled. The D/A converter **108** and the drive voltage control circuit **109** are included in the preparation control unit **16** of the sample preparation apparatus **3**.

In order to clean the piston **58** and the substitution container **57**, a cleaning fluid supplying unit **110** to which the cleaning fluid from the cleaning fluid unit **90** is supplied is provided at the lower side of the liquid surface detection sensor **82**. A cleaning fluid discharging unit **111** which leads from the bottommost part of the condensed sample holding chamber **80** to the outside of the substitution container **57** is provided. A cleaning fluid supplying/discharging unit **112** which leads from a bottom surface **68***a* of the holding chamber **68** to the outside of the substitution container **57** is provided. The cleaning fluid for performing additional cleaning to be described later (cleaning to be performed when the rotation of the rotor **72** is not sufficient) is supplied from the cleaning fluid supplying/discharging unit **112** and discharged. The cleaning fluid when cleaning the piston **58** and the substitution container **57** and the cleaning fluid when performing additional cleaning are discharged from the cleaning fluid discharging unit **111**.

Here, a process of the present embodiment in which the mixed solution of the biological samples and the preservative solution is discriminated and the liquid sample in which the concentration of the cells to be measured is increased is prepared from the liquid sample containing the cells to be measured which has been discriminated will be described in detail with reference to the pattern diagram of FIG. **14**.

As shown in FIG. **14**(*a*), the piston **58** is lowered so that the filter **60** moves downward from the upper side of the surface of the mixed solution of the biological samples and the preservative solution in the substitution container **57** to the solution.

Then, as shown in FIG. **14**(*b*), the liquid containing the cells to be measured (C**1**) (the first liquid) remains at the lower side of the filter **60** in the substitution container **57** and the liquid containing cells having a diameter smaller than that of the cells to be measured (C**2**) (the second liquid) remains at the upper side of the filter **60** (inside of the piston **58**).

Thereafter, as shown in FIG. **14**(*c*), the second liquid remaining in the piston **58** is discharged to the outside. In this

case, the second liquid is aspirated by applying a negative pressure to the inside of the piston **58**, and thus some of the cells to be measured (C**1**) contained in the first liquid are attached to the lower side of the filter **60**.

As shown in FIG. **14**(*d*), the cells to be measured attached to the lower side of the filter **60** are torn by rotating the rotor **72** and the cells to be measured contained in the first liquid are held in the condensed sample holding chamber. The measurement sample with a high concentration of the cells to be measured can be obtained by obtaining the liquid containing the cells to be measured held in the condensed sample holding chamber.

As shown in FIG. **13**, a taper **83** whose cross section gradually decreases toward the lower side is formed at the bottom of the condensed sample holding chamber **80**. The liquid sample held in the condensed sample holding chamber **80** is aspirated by the first pipette **26**A which is a liquid obtaining unit. At that time, the distal end of the first pipette **26**A is configured to lower to near the distal end of the taper **83** and to aspirate the liquid sample from near the distal end. Thus, the liquid sample can be used without waste by aspirating the liquid sample in the condensed sample holding chamber **80** as much as possible.

A tilt angle of a tilted surface **83***a* forming the taper **83** to the horizontal surface is not particularly limited in the present invention, and it is in the range of about 5 to 45 degrees taking into consideration the opening diameter at the distal end of the first pipette **26**A. The shape and accumulation of the horizontal section of the condensed sample holding chamber **80** can be determined taking into consideration the amount of the liquid sample required for measurement and a predetermined amount of yield.

[Processing Operation]

Next, the processing operation of the cell analyzer **1** mentioned above will be described.

FIGS. **15** and **16** are flow charts showing the process performed by each of the control units **8**, **16**, and **31** in the cell analyzer **1**.

In FIG. **15**, a process flow performed by the control unit (processing body) **31** of the data processing apparatus **4** is shown in the right column and a process flow performed by the measurement control unit **8** of the measurement apparatus **2** is shown in the left column. In FIG. **16**, a process flow performed by the preparation control unit **16** of the sample preparation apparatus **3** is shown in a line. The process flow is connected to the process flow of FIG. **15** at points A, B, and C. Hereafter, the processing content performed by the cell analyzer **1** will be described with reference to FIGS. **15** and **16**.

First, a control unit **31** of the data processing apparatus **4** displays a menu screen on the display **32** (step S**1**). Thereafter, when a measurement start instruction according to the menu screen is received from the input unit **33** (step S**2**), the control unit **31** of the data processing apparatus **4** sends a measurement start signal to the measurement apparatus **2** (step S**3**).

When receiving the measurement start signal (step S**4**), the measurement control unit **8** of the measurement apparatus **2** sends a preparation start signal to the sample preparation apparatus **3** (step S**5** and point A).

When receiving the preparation start signal (step S**6**), the preparation control unit **16** of the sample preparation apparatus **3** aspirates the reagent to be used for preparation of the measurement sample (stain solution, RNase) into a flow channel in the apparatus and allows the cell dispersion unit **25** to disperse cells in the mixed solution of the biological samples and the preservative solution containing methanol as a main ingredient held in the biological sample container **53** (steps S**7** and S**8**).

Thereafter, the preparation control unit **16** of the sample preparation apparatus **3** allows only a predetermined amount of the mixed solution after dispersion to be aspirated from the biological sample container **53** into the flow channel in the apparatus (step S**9**), sends the mixed solution to the substitution container **57** of the discrimination/substitution unit **29**, and makes the discrimination/substitution unit **29** perform the discrimination/substitution process of the mixed solution (step S**10**).

[Content of the Discrimination/Substitution Process]

FIGS. **17** and **18** are flow charts showing the discrimination/substitution process (step S**10**). In the discrimination/substitution process, the cells to be measured are discriminated from the other cells. At that time, the rotation of the rotor **72** which detaches the cells to be measured attached to the filter **60** is monitored, cleaning of a filtration unit (the substitution container **57**) is performed when the rotating speed is not sufficient, and rediscrimination (retry) of the cells to be measured is performed.

As shown in FIG. **17**, the preparation control unit **16** of the sample preparation apparatus **3** first initializes the count of additional cleaning of the filtration unit (step T**1**). Then, the preparation control unit **16** of the sample preparation apparatus **3** moves the sample pipetting unit **26** to the sample setting unit **24** (step T**2**) and makes the first pipette **26**A aspirate the mixed solution of the biological samples and the preservative solution in the biological sample container **53** set in the rotating table **24**A (step T**3**).

Then, the preparation control unit **16** moves the sample pipetting unit **26**A to the substitution container **57** (step T**4**) and makes the first pipette **26** discharge the mixed solution aspirated to the substitution container **57** (step T**5**).

Then, the diluted solution (substituted solution) is introduced from the diluting fluid unit **55** to the substitution container **57** via the valve V**6** (step T**6**).

Then, the piston **58** is moved downward up to a predetermined height for filtration by the driving unit **59** (step T**7**) and the mixed solution in the substitution container **57** is aspirated into the piston **58** and filtrated (step T**8**). At the time of aspiration and filtration, the valves V**10** and V**12** to which a relief valve is connected are used. In this case, the relief valve is set to −5 kpa. Thus, at the time of aspiration and filtration, a pressure of about −3 kpa is applied to the filter **60** arranged at the bottom end of the piston **58**. The liquid is aspirated and filtrated with such a weak negative pressure, and thus filtration can be performed without allowing the cells to be measured to pass the filter **60** and to be discharged to the discarding unit **61**.

Then, the piston **58** is moved to the lower side by the driving unit **59** (step T**9**) and the mixed solution in the substitution container **57** is aspirated into the piston **58** and filtrated, similar to step T**8** (step T**10**).

When the movement of the piston **58** and the aspiration and filtration of the sample are repeated at a predetermined number of times and the piston **58** moves to a predetermined lowest dead point (step T**11**), the mixed solution in the substitution container **57** is aspirated into the piston **58** and filtrated, similar to step T**8** (step T**12**). When the sensor unit **82***a* of the liquid surface detection sensor **82**, which is the capacitance type sensor, arranged in the substitution container **57** detects the liquid surface (step T**13**), the aspiration is stopped after a lapse of predetermined time (step T**14**). In this case, the liquid sample containing the cells to be measured is filled in

the holding chamber **68** arranged at the bottom of the substitution container **57** and the condensed sample holding chamber **80**.

Then, the positive pressure is applied to the piston **58** to remove cells (substances to be analyzed) blocked in the through holes of the filter **60** or attached to the lower surface of the filter **60** and return to the substitution container **57** (the holding chamber **68** and the condensed sample holding chamber **80**) (step T**15**).

Then, in step T**16**, the rotor **72** is rotated by making the driving motor **70***a* rotate the magnet **69** to remove the cells to be measured attached to the lower surface of the filter **60**, and the cells to be measured contained in the liquid sample in the holding chamber **68** are moved to the direction of the condensed sample holding chamber **80** to allow the cells to be measured to be held in the condensed sample holding chamber **80**.

In step T**16**, after a lapse of predetermined time (e.g. 3 seconds) after the start of rotation of the rotor **72**, the monitoring of the rotation of the rotor **72** is started by the rotation information acquiring unit **100** (step T**17**). As described above, the monitoring of the rotation is performed by detecting the light emitted from the light emitting unit **101** and reflected by the light reflecting unit **103** by the light receiving unit **102**.

Then, the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is lower than a predetermined lower limit threshold (step T**18**). When the set rotating speed is 1300 rpm, the lower limit threshold can be set to, for example, 800 rpm which is lower by 500 rpm than the set rotating speed. On the other hand, an upper limit threshold to be described later can be set to 1800 rpm which is higher by 500 rpm than the set rotating speed.

When determining that the rotating speed of the rotor **72** is lower than 800 rpm which is the predetermined lower limit threshold, the preparation control unit **16** advances the process to step T**19** and terminates the monitoring of the rotation of the rotor **72**.

Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**20**.

Then, the preparation control unit **16** determines whether or not the number of times of additional cleaning of the filtration unit is less than three times in step T**21**. When determining that the number of times of additional cleaning of the filtration unit is less than three times, the preparation control unit **16** performs the additional cleaning of the filtration unit (step T**22**). On the other hand, when determining that the number of times of additional cleaning of the filtration unit is three times or more, the preparation control unit **16** advances the process to step T**28** and sends an error message to the data processing apparatus **4** in step T**28**.

After completion of the additional cleaning of the filtration unit, the preparation control unit **16** counts up the additional cleaning of the filtration unit in step T**23**, returns to step T**6**, and allows the diluted solution (substituted solution) to be reintroduced from the diluting fluid unit **55** in the substitution container **57** via the valve V**6**. The processes after step T**7** as described above are repeated.

In step T**18**, when the preparation control unit **16** determines that the rotating speed of the rotor **72** is higher than the predetermined lower limit threshold ("NO" in step T**18**), the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is higher than a predetermined upper limit threshold in step T**24**.

When determining that the rotating speed of the rotor **72** is higher than 1800 rpm which is the predetermined upper limit threshold, the preparation control unit **16** advances the process to step T**25** and terminates the monitoring of the rotation of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**26**, advances the process to step T**27**, and sends the error message to the data processing apparatus **4** in step T**27**. On the other hand, when determining that the rotating speed of the rotor **72** is lower than 1800 rpm which is the predetermined upper limit threshold, the preparation control unit **16** advances the process to step T**29** and terminates the monitoring of the rotation of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**30** and advances the process to step T**31**.

The preparation control unit **16** moves the sample pipetting unit **26** to the substitution container **57** (step T**31**), makes the first pipette **26**A aspirate the condensed sample from the condensed sample holding chamber **80** (step T**32**), and moves the sample pipetting unit **26** to the sample setting unit (step T**33**).

Then, the preparation control unit **16** cleans the filtration unit (step T**34**). In this case, the cleaning fluid is supplied from the cleaning fluid supplying unit **110** for filters to the substitution container **57**.

The liquid sample mainly containing the cells to be measured (epithelial cells) in which the number of cells other than the cells to be measured is reduced can be obtained by the discrimination/substitution process. In the discrimination/substitution process, the concentration of methanol contained in the preservative solution in the liquid supplied from the biological sample container **53** to the substitution container **57** (the mixed solution of the biological samples and the preservative solution) can be diluted by substituting most of the preservative solution with the diluted solution. Thus, in a DNA staining process to be described later, the influence of the preservative solution can be reduced and DNA of the cells to be measured can be well stained.

In the discrimination/substitution process, since the substitution process of the preservative solution and the diluted solution can be performed while performing the discrimination process of cells, the discrimination process and the substitution process can be performed in a shorter time than when these two processes are performed separately.

In the discrimination/substitution process, the cells to be measured (epithelial cells) attached to the lower surface of the filter **60** are detached by the shearing force by rotating the rotor **72** to allow the detached cells to be suspended in the first liquid of the lower side of the filter **60**, and the cells to be measured (epithelial cells) blocked in the through holes of the filter **60** are removed by applying pressure from the upper side of the filter **60** to the through holes of the filter **60** to allow the cells to be suspended in the first liquid of the lower part of the filter **60**. Thus, the cells to be measured (epithelial cells) attached to the filter can be efficiently recovered without loss of them.

[Preparation of the Measurement Sample]

Returning to FIG. **16**, the preparation control unit **16** of the sample preparation apparatus **3** supplies the condensed sample from the sample pipetting unit **26** moved to the sample setting unit to the measurement sample container **54** (step S**11**).

Then, the preparation control unit **16** of the sample preparation apparatus **3** sends the stain solution and RNase stored in the apparatus from the reagent quantitating unit **28** to the second pipette **26**B, the second pipette **26**B supplies the stain solution and RNase which have been sent to the measurement sample container **54** (step S**12**) and produces the measurement sample by performing DNA staining and RNA process in the measurement sample container **54** (step S**13**).

After the completion of the process, the obtained measurement sample is quantified by the sample quantitating unit **27** through the first pipette **26**A and supplied to the detection unit **6** of the measurement apparatus **2** after quantification (step S**14** and point B).

The preparation control unit **16** of the sample preparation apparatus **3** always determines whether or not the shutdown signal from the measurement apparatus **2** is received (step S**15** and point C), returns to step S**6** for determining whether or not the preparation start signal is received when the signal is not received, and executes the shutdown to terminate the sample preparation process when the signal is received (step S**16**).

[Measurement by the Measurement Apparatus and its Data Analysis]

Returning to FIG. **15**, after sending the preparation start signal, the measurement control unit **8** of the measurement apparatus **2** always determines whether or not the measurement sample is supplied from the sample preparation apparatus **3** (step S**17**).

When the measurement sample is sent from the sample preparation apparatus **3** (point B), the control unit **8** of the measurement apparatus **2** sends the measurement sample to the flow cell **45** of a measurement unit **14**, performs the measurement of cells of the measurement sample (step S**18**), and sends the measurement data to the data processing apparatus **4** (step S**19**).

On the other hand, after sending the measurement start signal, the control unit **31** of the data processing apparatus **4** always determines whether or not the measurement data is received from the measurement apparatus **2** (step S**20**).

When receiving the measurement data from the measurement apparatus **2**, the control unit **31** of the data processing apparatus **4** analyzes the cells and nuclei using the measurement data and determines whether or not the cells in the measurement sample become cancerous (step S**21**).

The control unit **31** of the data processing apparatus **4** displays the analysis results on the display **32** (step S**22**) and determines whether or not a shutdown instruction is input by the user (step S**23**).

When the shutdown instruction is input, the control unit **31** of the data processing apparatus **4** sends a shutdown signal to the measurement apparatus **2** (step S**24**).

The control unit **8** of the measurement apparatus **2** always determines whether or not the shutdown signal from the data processing apparatus **4** is received (step S**25**), returns to step S**4** for determining whether or not the measurement start signal is received when the signal is not received, transfers the shutdown signal to the sample preparation apparatus **3** when the signal is received (step S**26**), and executes the shutdown to terminate the measurement process (step S**27**).

In the embodiments, the rotation of the rotor **72** is monitored, when performing the discrimination/substitution process, however, the present invention is not limited thereto. For example, when activating the apparatus or when terminating the measurement, the monitoring of the rotation of the rotor **72** can also be performed. When terminating the measurement, the time when the waiting time to the next measurement is long is included (for example, when there is a waiting time of 1 hour or more) except when terminating a daily measurement. Hereinafter, procedures for monitoring the rotation of the rotor **72** after the measurement (FIG. **19**) and at the time of activating the apparatus (FIG. **20**) will be described based on the flow charts.

After the Measurement (Adhesion-preventive Process)

FIG. **19** is a flow chart showing the procedure for monitoring the rotation of the rotor **72** after the measurement. When an interval until the next measurement is performed is long, for example, when terminating the daily measurement, an insufficient cleaning may cause the rotor **72** to adhere to the wall surface of the substitution container **57**. A normal operation of the rotor **72** at the next measurement can be ensured by checking the rotation of the rotor **72** after the measurement and performing the additional cleaning of the filtration unit, if necessary.

The process until the filtration unit is cleaned is the same as the process in the discrimination/substitution process described in FIGS. **17** and **18**. The preparation control unit **16** of the sample preparation apparatus **3** initializes the count (m=0) of additional cleaning of the filtration unit in step T**100** when cleaning the filtration unit.

When terminating the cleaning of the filtration unit, the preparation control unit **16** rotates the rotor **72** by making the driving motor **70***a* rotate the magnet **69** in step T**101**.

In step T**101**, after a lapse of predetermined time (e.g. 3 seconds) after the start of rotation of the rotor **72**, the monitoring of the rotation of the rotor **72** is started by the rotation information acquiring unit **100** (step T**102**). As described above, the monitoring of the rotation is performed by detecting the light emitted from the light emitting unit **101** and reflected by the light reflecting unit **103** by the light receiving unit **102**.

Then, the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is lower than a predetermined lower limit threshold (step T**103**). When the set rotating speed is 1300 rpm, the lower limit threshold can be set to, for example, 800 rpm which is lower by 500 rpm than the set rotating speed. On the other hand, an upper limit threshold to be described later can be set to 1800 rpm which is higher by 500 rpm than the set rotating speed.

When determining that the rotating speed of the rotor **72** is lower than 800 rpm which is the predetermined lower limit threshold, the preparation control unit **16** advances the process to step T**104** and terminates the monitoring of the rotation of the rotor **72**.

Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**105**.

Then, the preparation control unit **16** determines whether or not the number of times of additional cleaning of the filtration unit is less than three times in step T**106**. When determining that the number of times of additional cleaning of the filtration unit is less than three times, the preparation control unit **16** performs the additional cleaning of the filtration unit (step T**107**). On the other hand, when determining that the number of times of additional cleaning of the filtration unit is three times or more, the preparation control unit **16** advances the process to step T**113** and sends an error message to the data processing apparatus **4** in step T**113** (abnormal termination).

After completion of the additional cleaning of the filtration unit, the preparation control unit **16** counts up (m=m+1) the additional cleaning of the filtration unit in step T**108**, returns to step T**101**, and starts the rotation of the rotor **72** again. The processes after step T**102** as described above are repeated.

In step T**103**, when the preparation control unit **16** determines that the rotating speed of the rotor **72** is higher than the predetermined lower limit threshold ("NO" in step T**103**), the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is higher than a predetermined upper limit threshold in step T**109**.

When determining that the rotating speed of the rotor **72** is higher than 1800 rpm which is the predetermined upper limit threshold, the preparation control unit **16** advances the process to step T**110** and terminates the monitoring of the rota-

tion of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**111**, advances the process to step T**112**, and sends the error message to the data processing apparatus **4** in step T**112** (abnormal termination). On the other hand, when determining that the rotating speed of the rotor **72** is lower than 1800 rpm which is the predetermined upper limit threshold in step T**109**, the preparation control unit **16** advances the process to step T**114** and terminates the monitoring of the rotation of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**115**. Then, it is normally terminated.

At the Time of Activating the Apparatus

FIG. **20** is a flow chart showing the procedure for monitoring the rotation of the rotor **72** at the time of activating the apparatus. The measurement can be performed smoothly by checking the rotation state of the rotor **72** before activating the apparatus.

When a start switch is pushed by the user, initialization of the apparatus is performed in step T**200** and the count of additional cleaning of the filtration unit is also initialized (n=0).

When the initialization is terminated, the preparation control unit **16** rotates the rotor **72** by applying a predetermined voltage to the driving motor **70***a* to rotate the magnet **69** in step T**201**.

In step T**201**, after a lapse of predetermined time (e.g. 3 seconds) after the start of rotation of the rotor **72**, the monitoring of the rotation of the rotor **72** is started by the rotation information acquiring unit **100** (step T**202**). As described above, the monitoring of the rotation is performed by detecting the light emitted from the light emitting unit **101** and reflected by the light reflecting unit **103** by the light receiving unit **102**.

Then, the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is lower than a predetermined lower limit threshold (step T**203**). When the set rotating speed is 1300 rpm, the lower limit threshold can be set to, for example, 800 rpm which is lower by 500 rpm than the set rotating speed. On the other hand, an upper limit threshold to be described later can be set to 1800 rpm which is higher by 500 rpm than the set rotating speed. As for the lower limit threshold, the rotating speed for indexing whether or not the rotor is adhering may be set as a threshold. In the present embodiment, when the rotating speed of the rotor is 800 rpm or less, there is a possibility that the rotor is adhering. Thus, the lower limit threshold is set to 800 rpm.

When determining that the rotating speed of the rotor **72** is lower than 800 rpm which is the predetermined lower limit threshold, the preparation control unit **16** advances the process to step T**204** and increases the drive voltage of the driving motor **70***a* depending on a predetermined determination value, for example, a ratio obtained by dividing the set rotating speed of the rotor **72** by an actual rotating speed of the rotor **72** (the actual number of rotation) in step T**204**. In this case, since the ratio becomes higher with a lower actual rotating speed than the set rotating speed, the control to increase an amount of increase of the drive voltage of the driving motor **70***a* is performed with a higher level of the ratio.

Then, the preparation control unit **16** determines whether or not the drive voltage of the driving motor **70***a* increased in step T**204** reaches the upper limit in step T**205**. When determining that the drive voltage of the driving motor **70***a* increased in step T**204** reaches the upper limit, the preparation control unit **16** advances the process to step T**206** and terminates the monitoring of the rotation of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**207** and advances the process to step T**208**. On the other hand, when determining that the drive voltage of the driving motor **70***a* does not reach the upper limit, the preparation control unit **16** returns to step T**202**. The rotation of the rotor **72** is continuously monitored, and the processes after step T**203** as described above are repeated.

Then, the preparation control unit **16** determines whether or not the number of times of additional cleaning of the filtration unit is less than three times in step T**208**. When determining that the number of times of additional cleaning of the filtration unit is less than three times, the preparation control unit **16** performs the additional cleaning of the filtration unit (step T**209**). On the other hand, when determining that the number of times of additional cleaning of the filtration unit is three times or more, the preparation control unit **16** advances the process to step T**213** and sends an error message to the data processing apparatus **4** in step T**213** (abnormal termination).

After completion of the additional cleaning of the filtration unit, the preparation control unit **16** counts up (n=n+1) the additional cleaning of the filtration unit in step T**210**, returns to step T**201**, and starts the rotation of the rotor **72** again. The processes after step T**202** as described above are repeated.

In step T**203**, when the preparation control unit **16** determines that the rotating speed of the rotor **72** is higher than the predetermined lower limit threshold ("NO" in step T**203**), the preparation control unit **16** determines whether or not the detected rotating speed of the rotor **72** is higher than a predetermined upper limit threshold in step T**211**.

When determining that the rotating speed of the rotor **72** is higher than 1800 rpm which is the predetermined upper limit threshold, the preparation control unit **16** advances the process to step T**212** and decreases the drive voltage of the driving motor **70***a* depending on a predetermined determination value, for example, a ratio obtained by dividing the set rotating speed by an actual rotating speed of the rotor **72** (the actual number of rotation) in step T**212**. In this case, the ratio becomes lower with a higher actual rotating speed than the set rotating speed. However, contrary to step T**204**, the control to increase an amount of decrease of the drive voltage of the driving motor **70***a* is performed with a lower level of the ratio. Then, the process is returned to step T**202**, the rotation of the rotor **72** is continuously monitored, and the processes after step T**203** as described above are repeated.

On the other hand, when determining that the rotating speed of the rotor **72** is lower than 1800 rpm which is the predetermined upper limit threshold in step T**211**, the preparation control unit **16** advances the process to step T**214** and terminates the monitoring of the rotation of the rotor **72**. Then, the preparation control unit **16** terminates the rotation of the rotor **72** in step T**215**. Then, it is normally terminated.

In the example shown in FIG. **20**, the rotation of the rotor **72** can be normally maintained by controlling the drive voltage to the driving motor **70***a* based on the rotating speed which is the rotation information of the rotor **72** and performing the additional cleaning of the filtration unit.

[Other Variants]

The disclosed embodiments are illustrative and not restrictive. The scope of the present invention is defined by the attached claims rather than by the embodiments, and all changes equivalent to the configurations of claims are enclosed therein.

For example, in the embodiment, the reflected light is detected by the outer end surface of the light reflecting unit **103** having a bar shape embedded in the rotor **72**, but the rotation information can also be acquired by forming a pass-through hole in the peripheral surface of the rotor **72** and

detecting the light emitted from the light emitting unit **101** by the light receiving unit **102** via the pass-through hole of the rotor **72** during rotation. In this case, the light emitting unit **101** and the light receiving unit **102** are arranged in a position facing each other with the rotor **72** in between.

In the embodiments, a member having a bar shape is used as the light reflecting unit, but a member in which a metal having a sheet or film shape is adhered to the peripheral surface of the rotor **72** can also be used as the light reflecting unit.

In the embodiments, the rotor **72** rotating is irradiated with light and the reflected light from the rotor **72** is detected, but the rotation information of the rotor **72** can also be acquired by providing a light-emitting element in the rotor **72** itself and detecting the light from the light-emitting element.

In the embodiments, the rotation information of the rotor **72** is acquired using light, but the information related to the rotational state of the rotor **72** can also be acquired by detecting a flow of the liquid sample in the substitution container generated by rotating the rotor **72**.

The information related to the rotation of the rotor **72** can also be acquired using ultrasonic waves or radars.

The information related to the rotation of the rotor **72** can also be acquired by detecting a magnetic field generated by the rotation of the rotor **72** with a magnetic sensor.

In addition to the capacitance type sensor, a photoelectric sensor and an ultrasonic sensor can be appropriately employed as a liquid surface detecting means for detecting the surface of the liquid in the substitution container **57**. In the case of the photoelectric sensor, the surface of the liquid in the substitution container **57** can be detected without allowing a sensor unit to project to the substitution container **57**.

In the embodiments, the epithelial cells of the uterine cervix are used as the cells to be measured, but the malignant transformation of buccal cells, epithelial cells of the bladder and the pharynx, and epithelial cells of organs can be determined.

In the embodiments, the liquid sample is separated into the first liquid and the second liquid by applying the negative pressure to the piston **58** so as to move the piston **58** to the lower side following the lowering of the surface of the first liquid, but the liquid sample may be separated into the first liquid and the second liquid by sealing between the upper opening portion in the substitution container **57** and the piston **58** to which the filter **60** is fixed with a sealing member and moving the piston **58** to the lower side by the driving unit **59**. The cells to be measured contained in the first liquid held in the holding chamber **68** are moved to the condensed sample holding chamber **80** by rotating the rotor **72**, and then the liquid sample present in the condensed sample holding chamber **80** may be obtained. Thus, only cells, such as red blood cells and white blood cells, except the epithelial cells which are the cells to be measured pass the filter **60**, while the epithelial cells which are the cells to be measured do not pass the filter **60** and are held in the holding chamber **68**. Thus, the liquid in which the number of cells other than the cells to be measured is reduced can be obtained.

In the embodiments, the measurement sample prepared by the sample preparation apparatus **3** is measured by the flow cytometer, but a smeared specimen preparing apparatus which smears the measurement sample prepared by the sample preparation apparatus **3** on a slide glass to prepare a smeared specimen and a cell image processing apparatus which images the smeared specimen prepared and analyzes epithelial cells in the imaged image may be provided. Since the measurement sample in which the concentration of the epithelial cells which are the cells to be measured is increased and the number of cells, such as red blood cells and white blood cells, is reduced is smeared on the slide glass, the epithelial cells can be analyzed with sufficient accuracy.

In the embodiments, the rotor **72** is rotated after applying pressure from the upper side of the filter **60** to the through holes of the filter **60**, but the pressure may be applied from the upper side of the filter **60** to the through holes of the filter **60** after rotating the rotor **72**. In the embodiments, the rotor **72** is rotated while applying pressure to the through holes of the filter **60**, but the rotor **72** may be rotated after completion of applying pressure to the through holes of the filter **60**.

In the embodiments, the control of the drive voltage to the driving motor **70***a* is performed at the time of activating the apparatus, but the present invention is not limited thereto, the control of the drive voltage to the driving motor **70***a* may be performed based on the rotating speed acquired by the monitoring of the rotation in checking at the time of measurement (retry process) and after the measurement (adhesion-preventive process).

What is claimed is:

1. A sample preparation apparatus comprising:

a filter comprising a plurality of holes having a first diameter configured to separate predetermined cells having a second diameter larger than the first diameter from a liquid sample containing a plurality of types of cells, the predetermined cells being trapped on a surface of the filter;

a rotor which includes a magnetic body, the rotor being provided to face to the surface of the filter;

a driving unit which is configured to rotate the rotor using a magnetic force;

a rotation information acquiring unit which is configured to acquire rotation information of the rotor when the driving unit rotates the rotor;

a holding chamber sidewall defining a holding chamber which is configured to hold the rotor and an opening along an outer circumference of the holding chamber; and

a condensed sample holding chamber attached to the holding chamber at the opening such that the condensed sample holding chamber is disposed adjacent to the outer circumference of the sidewall of the holding chamber,

wherein the rotor is configured to move the predetermined cells from the holding chamber to the condensed sample holding chamber.

2. The apparatus of claim **1**, wherein

the rotation information acquiring unit includes a light emitting unit which irradiates the rotor with light and a light receiving unit which detects the light emitted from the light emitting unit

and acquires the rotation information based on a light information detected by the light receiving unit.

3. The apparatus of claim **2**, wherein

the rotor includes a light reflecting unit which reflects the light

and the light receiving unit detects light from the light emitting unit reflected by the light reflecting unit during rotation of the rotor.

4. The apparatus of claim **3**, wherein

the rotor has a circular cylindrical shape

and the light reflecting unit is embedded in a concave portion formed in the peripheral surface of the rotor.

5. The apparatus of claim **1**, wherein

the rotation information acquiring unit acquires a rotating speed of the rotor per a predetermined time as the rotation information.

6. The apparatus of claim 1, wherein
the driving unit is controlled based on the rotation information of the rotor acquired by the rotation information acquiring unit.

7. The apparatus of claim 6, wherein
a driving force of the driving unit is increased when the rotating speed of the rotor is lower than a predetermined threshold.

8. The apparatus of claim 6, wherein
a driving force of the driving unit is decreased when the rotating speed of the rotor is higher than a predetermined threshold.

9. The apparatus of claim 1, wherein
the acquired rotation information of the rotor is the rotating speed of the rotor per the predetermined time
and the driving unit is controlled so that the rotating speed of the rotor is within a predetermined rotating speed range.

10. The apparatus of claim 1, further comprising
a control unit which controls the driving unit based on the rotation information of the rotor acquired by the rotation information acquiring unit.

11. The apparatus of claim 1, wherein
the driving unit includes a driving magnetic body which attaches the rotor with the magnetic force and a driving source which rotates the driving magnetic body.

12. The apparatus of claim 1, further comprising:
a cell obtaining unit which obtains the predetermined cells detached by the rotor; and
a sample preparation unit which prepares a measurement sample from the predetermined cells obtained by the cell obtaining unit and a predetermined reagent.

13. The apparatus of claim 12, wherein
the rotation information acquiring unit rotates the rotor to acquire the rotation information of the rotor at the time of completing measurement using the prepared measurement sample.

14. The apparatus of claim 1, further comprising
a cleaning unit which cleans the rotor.

15. The apparatus of claim 13, wherein
the acquired rotation information of the rotor is the rotating speed of the rotor per the predetermined time, and
the cleaning unit starts cleaning of the rotor when the rotating speed of the rotor is lower than the predetermined threshold.

16. The apparatus of claim 1, wherein
the rotation information acquiring unit rotates the rotor to acquire the rotation information of the rotor at the time of activating the apparatus.

17. The apparatus of claim 1, wherein
the rotation information acquiring unit acquires the rotation information of the rotor at the time of detaching the predetermined cells by the rotor.

18. The apparatus of claim 1, wherein
the filter separates cells of uterine cervix as the predetermined cells from a liquid sample containing a plurality types of cells.

19. The apparatus of claim 1, wherein the condensed sample holding chamber is arranged in a periphery part of the holding chamber.

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